TO STUDY THE PREVALENCE OF OSTEOPOROSIS AND THE EFFICACY AND SAFETY OF ANTIRESORPTIVE THERAPY IN CKD3-5D PATIENTS

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BY

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(MAY, 2020)

DECLARATION

I declare that the thesis entitled "**TO STUDY THE PREVALENCE OF OSTEOPOROSIS AND THE EFFICACY AND SAFETY OF ANTIRESORPTIVE THERAPY IN CKD3-5D PATIENTS**" has been prepared by me under the guidance of **Dr. Vikas Makkar**, Professor & Head, Department of Nephrology, Dayanand Medical College and Hospital, Ludhiana. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

my family

&

Teachers

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ABBREVIATIONS

ALP:	Alkaline phosphatase
BMD:	Bone mineral density
CG:	Cockcroft Gault
Dmab:	Denosumab
DEXA:	Dual energy X-ray absorptiometry
GFR:	Glomerular filtration rate
PTH:	Parathyroid hormone
KDIGO:	Kidney Disease Improving Global Outcomes
sCr:	Serum creatinine

ABSTRACT

Background: Changes in bone and mineral metabolism occur during the course of CKD. The prevalence of low bone mineral density (BMD) and osteoporosis increases with greater severity of chronic kidney disease (CKD). Low BMD predicts the fracture risk in the general population. Bisphosphonate therapy improves BMD and lowers the fracture risk in general population. In this study, the effect of oral alendronate on BMD in patients with CKD 3-5D is evaluated.

Material and Methods: Eighty patients of CKD 3- 5D stage were divided into two equal groups, one who received 35 mg alendronate, taken once a week for 12 months compared with another group which did not receive alendronate. Lumbar spine, femur neck and total hip BMD were measured by dual energy X-ray absorptiometry at baseline, 6 months and 12 months. Parathyroid hormone, calcium, phosphorous and alkaline phosphatase levels were assayed at baseline and at 1, 3, 6 and 12 months.

Results: There was improvement in mean T score, Z score and BMD at level of lumbar spine, femur neck and total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of T score, Z score and BMD was statistically significant between two groups at 6 and 12 month irrespective of CKD stage. There was no major adverse effect of the therapy except mild GI intolerance.

Conclusions: Low-dose alendronate, administered for longer duration, appears to be well tolerated in CKD 3-5D patients. The BMD, T-scores and Z score declined in the placebo group over 12 months, while there was improvement in the treatment group, suggesting a bone-preserving effect of alendronate. Further studies of longer duration, and including examination of bone histology, are needed to assess whether bisphosphonates can be used to preserve BMD in CKD 3-5D patients.

KEY WORDS: Alendronate, Bone mineral density, DEXA scan.

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INTRODUCTION

Changes in bone and mineral metabolism occur early in the course of CKD. The prevalence of low bone mineral density (BMD) and osteoporosis increases with greater severity of chronic kidney disease (CKD). These changes are called Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD), which includes renal osteodystrophy, extraskeletal (vascular) calcification related to abnormalities of bone mineral metabolism. KDIGO recommended that the term, renal osteodystrophy, be exclusively used to define bone pathology associated with CKD. KDIGO recommended the term chronic kidney disease-mineral and bone disorder (CKD-MBD) be used to describe the much broader systemic disorder that occurs as a result of CKD.

CKD-MBD is a systemic disorder that develops in the course of CKD and may manifest by one or more of the following:

● Abnormalities of calcium, phosphorus, parathyroid hormone (PTH), or vitamin D metabolism

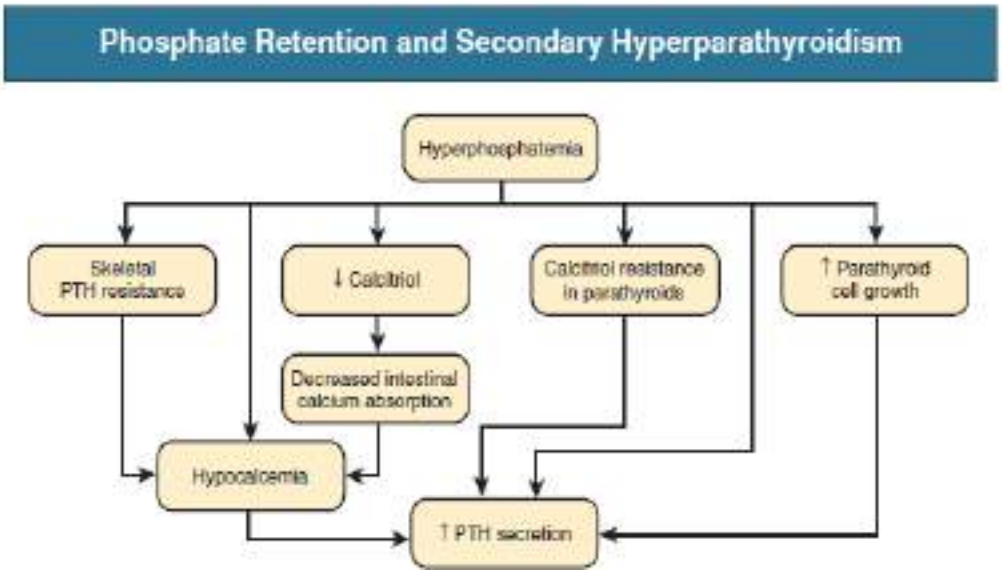
● Abnormalities in bone turnover, mineralization, volume linear growth, or strength

● Vascular or other soft-tissue calcification

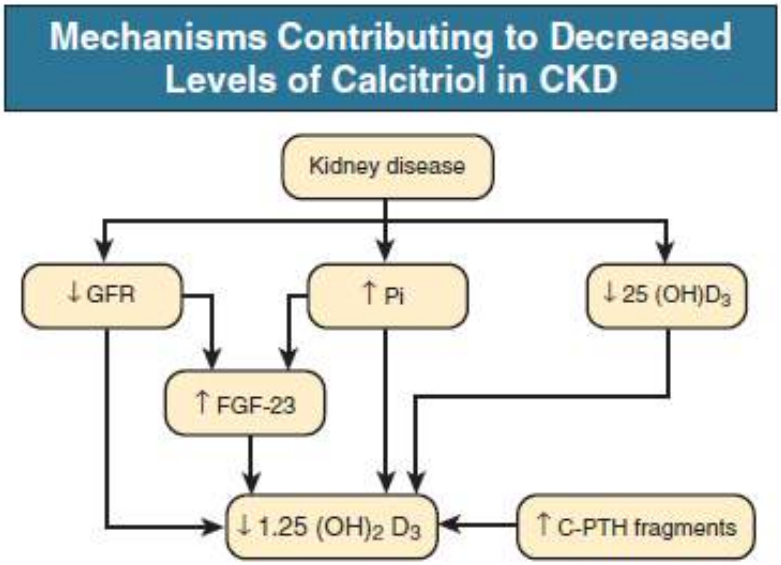
Renal osteodystrophy is the component of CKD-MBD that is identified and quantified through bone histomorphometry and includes osteitis fibrosa (hyperparathyroidism), adynamic bone disease and osteomalacia. Several factors related to the pathophysiology of CKD-MBD have been described as markers of increased cardiovascular risk and mortality in these patients, such as hyperparathyroidism, increased FGF-23 (Fibroblast Growth Factor-23) and metabolic acidosis. Metabolic disturbances associated with CKD are increased PTH, decreased 25-hydroxyvitamin D, decreased calcitriol, metabolic acidosis, increased bone alkaline phosphatase, hyperphosphatemia (late disorder), hypocalcemia (late disorder), increased FGF-23 (fibroblast growth factor-23). The elevation in serum PTH is observed from early stages of CKD and results in increased bone resorption in order to maintain calcium balance. Chronic PTH hypersecretion is

related to high turnover bone disease, with increased risk of fractures and bone deformities. Several factors contribute to hyperparathyroidism. The decreased pool of functioning nephrons results in limited capacity for calcitriol production (the active form of vitamin D), due to the smaller amount of 1α-hydroxylase, the enzyme responsible for the conversion of 25-hydroxyvitamin D (25OHD) in its active form. CKD patients, even at early stages of the disease, also have a higher prevalence of vitamin D insufficiency/deficiency than that found in the general population. The decrease in intestinal calcium absorption leads to PTH hyper secretion. The reduced expression of vitamin D receptor (VDR) and calcium-sensitive (CaR) receptor, increasing bone resistance to PTH action and stimulating its secretion, is also observed.

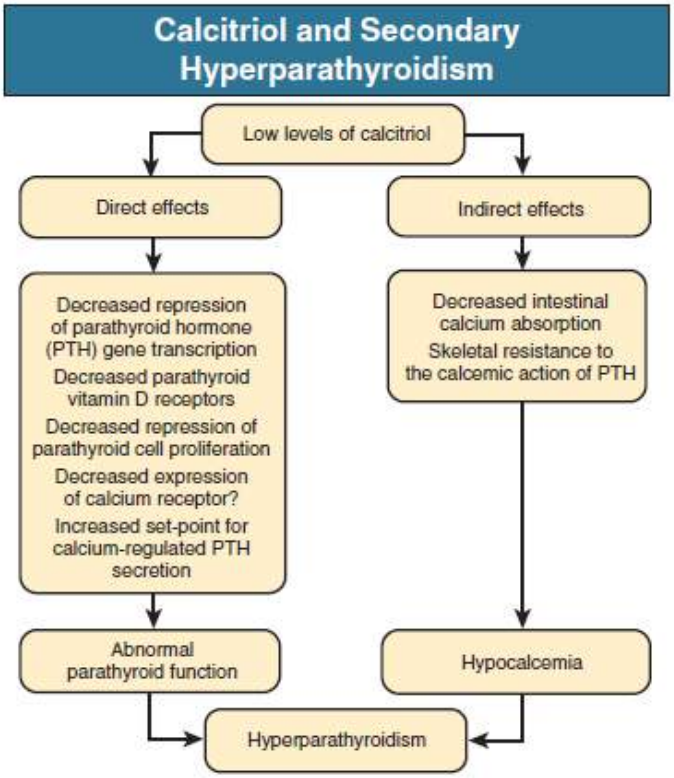
FGF-23 is a phosphatonin produced by osteoblasts and osteocytes which rises very early in CKD to counterbalance phosphate retention. FGF-23 causes inhibition of 1α-hydroxylase, contributing to reduced calcitriol synthesis and to secondary hyperparathyroidism. Increased serum phosphate further reduces calcitriol synthesis and can precipitate in vessels and soft tissues with calcium, reducing the ionized calcium fraction (indirectly stimulating the PTH secretion).



Role of phosphate retention in the pathogenesis of secondary hyperparathyroidism



Mechanisms contributing to decreased levels of calcitriol in CKD.


Calcitriol and Secondary Hyperparathyroidism
Low levels of calcitriol
Direct effects
Indirect effects
Decreased repression of parathyroid hormone (PTH) gene transcription
Decreased parathyroid vitamin D receptors
Decreased repression of parathyroid cell proliferation
Decreased expression of calcium receptor?
Increased set-point for calcium-regulated PTH secretion
Decreased intestinal calcium absorption
Skeletal resistance to the calcemic action of PTH
Abnormal parathyroid function
Hypocalcemia
Hyperparathyroidism

Role of low levels of calcitriol in the pathogenesis of secondary hyperparathyroidism.

Most large-scale studies to determine the effectiveness and safety of osteoporosis drugs or Antiresorptive therapy in the general population did not include patients with severe renal impairment (GFR<30 ml/min/1.73m2) as their safety was concern in severe renal impairment. The consensus-KDIGO 2012 reports safety and efficacy of these drugs in patients with CKD 1-3 without evidence of CKD-MBD, but does not guarantee their use in patients with GFR< 30 ml/min/1.73 m2, or those with metabolic disturbances of CKD-MBD, recommending to assess the potential benefit to risk of the prescription in this population. But recent studies and new RCTs recommended the safety and benefit of various anti resorbtive therapies in stage CKD 4-5 also. The recent consensus KDIGO 2017 guidelines also recommended the use of Antiresorptive therapy on BMD in end stage renal disease. So this study was done to study the efficacy and safety of Antiresorptive therapy in CKD3-5D patients and to study the prevalence of osteoporosis in patients with CKD3-5D.

AIMS AND OBJECTIVES

1. To study the prevalence of osteoporosis in CKD 3-5D patients
2. To study the effect of antiresorptive therapy on bone mineral density (BMD) in CKD 3-5D patients
3. To assess the adverse reactions of antiresorptive agent in CKD 3-5D patients

REVIEW OF LITERATURE

Many complications of CKD are initiated at early stages of the disease, among which the disturbances in bone metabolism.[1] At any age, these patients have increased risk of fragility fractures.[2] Klawansky and cols.[3] observed that osteopenia and osteoporosis were more common in patients with moderate (GFR 35-60 ml/min/1.73 m2) or severe (GFR <35 ml/min/1.73 m2) renal impairment. Cunningham and cols reported that osteoporosis is more common in patients with renal impairment than in the general population.[4]

DEXA is the main method used in the diagnosis and treatment of osteoporosis in the general population, as it measures bone mass and determines the risk of fractures. Despite the accuracy of DEXA in the diagnosis and prediction of fractures in the general population, studies in CKD patients fail to demonstrate its ability in determining bone disease.[5-10] In addition, some doubts persist on the most adequate osteoporosis drugs to be employed in patients with renal impairment.[11] Jassal and cols.[6] also reported positive correlation between GFR and BMD. In one study done by Lima and cols.[10], there was positive correlation between BMD and kidney function, but no correlation between DEXA and fractures. Transiliac bone biopsy with double tetracycline labeling has been the method of choice to define the type and severity of bone disease in CKD-MBD. However, it is an invasive method justified only in specific situations, usually in the more advanced forms of kidney disease.[12] Most of RCTs have used DEXA scan in evaluation of BMD in CKD. The 2017 revised KDIGO CKD-MBD recommendations in patients with CKD G3a–G5D with evidence of CKD-MBD and/or risk factors for osteoporosis, suggest BMD testing to assess fracture risk if results will impact treatment decisions.[13]

Recommendation of international consensus of KDIGO CKD work group 2012 is to maintain the levels of serum calcium, phosphorus and 25OH vitamin D within the normal range for patients with CKD stages 3-5.[1] Measures such as adequacy of phosphorus and protein intake, use of phosphate binders, vitamin D supplementation with pro-active

(ergo or cholecalciferol) and/or active (calcitriol) are required. Replacement of vitamin D (ergocalciferol or cholecalciferol), aiming to correct hypovitaminosis D and minimize hyperparathyroidism, is indicated as in the general population. In individuals with severe renal impairment, decreased 1α-hydroxylase enzyme can reduce the effectiveness of ergo or cholecalciferol replacement, making sometimes necessary the use of calcitriol. This agent is important to re-establish optimal calcium and phosphorus levels and minimize hyperparathyroidism, but should be prescribed with caution because of the risk of hypercalcemia, hyperphosphatemia, vascular calcification and adynamic bone disease.[14,15] In moderate to severe CKD patients on conservative treatment, serum PTH should be maintained in the upper limit (2-6 times of normality). When PTH levels are very high, resulting in high turnover disease (osteitis fibrosa), there is an increased rate of bone resorption and fracture risk. When PTH levels are suppressed, resulting in low turnover disease (adynamic bone disease), there is also an increased risk of fractures due to low bone formation. Moreover, in CKD patients, an accumulation of N-terminal portion of PTH, especially in dialysis patients, may overestimate its serum level.[16] The PTH therapeutic target in pre-dialysis patients is not known. KDIGO consensus suggests that in patients with GFR < 45 ml/min/1,73 m2 and PTH above the normal value, efforts to adequacy of serum phosphorus, calcium and 25OHD are priority to the absolute values of PTH. Attempts to normalize serum ionized calcium/calcium corrected for albumin, phosphorus, 25OHD and alkaline phosphatase (marker of bone turnover) are more important than the absolute values of PTH, even if they are above normal limits. The recent consensus KDIGO 2017 guidelines also recommended the use of Antiresorptive therapy on BMD in end stage renal disease.[11]

BISPHOSPHONATES

These antiresorptive agents, widely used in the treatment of osteoporosis, have been evaluated in patients with low GFR. Bisphosphonates are synthetic pyrophosphate analogues and were developed in the middle of this last century as growth inhibitors and

subsequently they were found to decrease bone resorption too. Bisphosphonates that do not contain nitrogen (etidronate, clodronate and tiludronate), considered “first-generation bind ATP which, when incorporated in osteoclasts, are cytotoxic to these cells, disrupting cell function and causing apoptosis. Nitrogenous bisphosphonates, called “second and third generation” (pamidronate, alendronate, ibandronate, risedronate and zolendronate) are more potent than their predecessors. They inhibit farnesyl pyrophosphatase synthase and other final steps of the intracellular mevalonate pathway whose end product is cholesterol.

UTILITY OF BISPHOSPHONATES IN PATIENTS WITH CKD

- Prevention and treatment of decreased bone mass after kidney transplantation
- Treatment of decreased bone mass in advanced CKD or dialysis
- Treatment of hypercalcaemia
- Treatment of calciphylaxis
- Prevention and treatment of vascular calcifications

Most large-scale studies to determine the effectiveness and safety of osteoporosis drugs in the general population did not include patients with severe renal impairment (GFR < 30 ml/min/1.73 m2).[14] Data about the long term use of Antiresorptive therapy in people with renal impairment come from two main studies where oral bisphosphonates were used. These Antiresorptive agents, widely used in the treatment of osteoporosis, have been evaluated in patients with low GFR.[14] The study by Miller et al[17], was based on an analysis of data from nine placebo controlled clinical trials of risedronate in 8996 osteoporotic women. In this combined data from nine randomizeed, double-blind, placebo-controlled phase III risedronate trials was analyzed.[18-51] The patients in these studies had no markedly abnormal laboratory parameters that were considered clinically significant and no evidence of significant disease. This analysis included the patients who received placebo (*n*=4500) or risedronate 5mg (*n*=4496) for up to 3 years (average duration of exposure, 2 years) and who had renal impairment (creatinine clearance [CrCl] < 80 ml/min). CrCl was estimated by the

Cockcroft and Gault method, based on age, weight, and serum creatinine. Of the 9883 patients evaluated in the primary intent-to-treat analysis, 8996 (91%) had some degree of renal impairment. Renal impairment was classified as severe in 572 (7%), moderate in 4071 (45%), and mild in 4353 (48%). Within each renal impairment subgroup, the two treatment groups (placebo and risedronate 5mg) were very similar with respect to baseline demographic and disease characteristics. Similar percentages of patients in the two treatment groups were categorized as having severe, moderate, or mild renal impairment. In both treatment groups, the patients with the most severe renal impairment were older, more frail, and had more severe osteoporosis. At baseline, the overall median (interquartile range) creatinine clearance was 49.5 (40.0–59.6) ml/min (range, 14.1–79.9 ml/min) for the placebo group and 49.2 (39.7–59.5) ml/min (range, 13.2–79.9 ml/min) for the risedronate 5mg group. Mean PTH levels at baseline were similar in the placebo and risedronate 5mg treatment groups and were within the normal range. For all patients with severe renal impairment for whom baseline PTH data were available, PTH levels were within the normal range.

The percentages of patients who discontinued increased with the severity of renal impairment; however, within each renal impairment subgroup, the percentages of patients who withdrew were similar in the risedronate and placebo groups. The most commonly cited reason for discontinuation was voluntary withdrawal (19% in the placebo group and 18% in the risedronate group), followed by adverse events (17% in each treatment group). A total of 5023 patients completed the trial and were included in the per protocol “sensitivity” analysis. The overall mean (SD) duration of treatment in these patients was 34 (±6.1) months. The results of the per protocol analyses were consistent with those of primary intent-to-treat analysis. The incidence of overall, urinary- and renal function–related, and specific renal function–related adverse events was similar within and between treatment groups in the subgroups of patients with severe, moderate, or mild renal impairment. Statistically and clinically, there were no significant differences. The

most common urinary-and renal function-related adverse event was urinary tract infection, which was noted in 10–13% in each treatment group in each renal impairment subgroup. The differences between the placebo and risedronate 5mg groups in the changes from baseline in serum creatinine at 6, 12, or 24 months or at the endpoint were not significant in any of the renal impairment subgroups. Although there were sporadic statistically significant differences between the treatment groups with respect to the mean percent changes from baseline in serum calcium and serum phosphorus, these differences were small and an expected consequence of changes in calcium homeostasis during therapy and were not considered to be clinically meaningful. These differences were small, early, transient, and asymptomatic and required no intervention. The mean percent increase from baseline to endpoint in BMD at the lumbar spine and femoral neck and trochanter was significantly greater in the risedronate 5mg group than in the placebo group in all three renal impairment subgroups, except at the femoral neck in the severe renal impairment subgroup. Mean percent changes (SD) from baseline to endpoint in lumbar spine BMD were −1.37% (1.72%) in the placebo group versus +4.23% (1.82%) in the risedronate group in patients with severe renal impairment; −0.47% (0.50%) in the placebo group versus +4.33% (0.51%) in the risedronate group in patients with moderate renal impairment; and −0.14% (0.19%) in the placebo group versus +3.96% (0.18%) in the risedronate group in patients with mild renal impairment ($p < 0.001$ for all comparisons).

The increases from baseline in BMD were greater in the risedronate 5 mg group than in the placebo group at all three skeletal sites at 6, 12, and 24 months in each renal impairment subgroup. In addition, the incidence of new vertebral fractures in the risedronate 5mg group was significantly lower than that in the placebo group within each renal impairment subgroup. The incidence of new vertebral fractures in risedronate-treated patients was similar across renal impairment subgroups (p =0.124), whereas the incidence in placebo-treated patients increased significantly with the severity of renal impairment ($p < 0.001$). Histomorphometric data from paired biopsy samples

(baseline and end of treatment) were available for 57 subjects with mild (placebo, n=22; risedronate, n=21) or moderate (placebo n=6; risedronate, *n*=8) renal impairment. The mean (SD) ages of these 57 subjects were 66 (9.1) years in the placebo group and 65 (10.8) years in the risedronate group. The mean (SD) serum creatinine levels were 1.03 (0.142) mg/dl in the placebo group and 1.02 (0.127) mg/dl in the risedronate group, and the median (range) calculated creatinine clearances were 60.2 (35.1–78.7) ml/min in the placebo group and 54.1 (41.5–78.9) ml/min in the risedronate group. In these renally impaired patients, risedronate treatment led to decreases from baseline of 68% in mineralizing surface and 54% in activation frequency Bone turnover marker data were available for a subgroup of the patients in the analysis (20–30% of the intent to-treat population, depending on the trial). As expected, the decreases from baseline in serum bone alkaline phosphatase levels and in urinary deoxypyridinoline/creatinine ratios were greater than those in the placebo group in all three renal impairment subgroups (data not shown). Importantly, the difference between the placebo and risedronate treatment groups in the severe renal impairment group was no greater than those in the mild and moderate renal impairment subgroups for either bone turnover marker.

Overall it was concluded that risedronate 5mg daily was safe and effective in the studied population, even in those with CrCl of 15-30ml/min.

Jamal et al.[52] used data from 6458 subjects from the Fracture Intervention Trial. This was a placebo controlled randomized clinical trial of alendronate in post menopausal women.[53-69] The renal function was estimated, using Cockcroft Gault, for these subjects allowing them to be categorized as having severely reduced renal function (CrCl <45mL/min) or moderately reduced or normal renal function (>45mL/min). Of the 6458 women that were studied, 581 women (9.9%) had an eGFR of <45 ml/minute, and 2409 (37.3%) had an eGFR between 45 and 59 ml/minute. Note that they did not find any difference in outcomes among subjects with an eGFR of 45–59 ml/minute and those with an ≥ eGFR of 60 ml/minute. As a result,

these groups were pooled, and the pooled data are presented. Compared with women with an eGFR ≥ 45 ml/minute, women with an eGFR <45 ml/ minute were significantly older, weighed less, had lower BMD at the hip and spine, had a greater prevalence of vertebral fractures, reported more fractures after 45 years of age, had poorer self-rated health, and had a higher serum creatinine at study entry.

Compared with placebo-treated women, alendronate increased total hip BMD by 4.9 ± 8.7% over a mean follow up of 3 years. Women with a reduced eGFR had a 5.6% (95% CI: 4.8–6.5) increase in total hip BMD compared with 4.8% (95% CI: 4.6–5.0) among women with normal to moderate renal dysfunction (interaction: p=0.04). Compared with placebo, alendronate increased spine BMD by 6.6 ± 5.8%, but in contrast to effects on hip BMD, there was no significant interaction between renal function and the increase in BMD (interaction: p=0.75). Similarly, there was no significant interaction between renal function and the increase in femoral neck (p=0.32). Among women with osteoporosis, the annualized percent changes in total hip, femoral neck, and spine BMD were similar among those with a CrCl <45 ml/minute and those with CrCl ≥ 45 ml/minute, with no evidence of an interaction between renal function and treatment assignment. Among all subjects followed for an average of 4 years, there were 907 clinical fractures, including 76 hip fractures. Women with reduced eGFR were also at an increased risk of any clinical fracture (OR=1.3; 95% CI: 1.0–1.6) and at increased risk of spine fractures (OR=2.5; 95% CI: 1.6–3.9) compared with women with an eGFR of ≥45 ml/ minute. Compared with placebo-treated women, alendronate reduced the risk of clinical fractures (OR 0.8; 95% CI: 0.70–0.9) regardless of renal function. Furthermore, treatment with alendronate reduced the risk of clinical fractures to a similar degree in those with (OR: 0.78; 95% CI: 0.51–1.21) and without reduced renal function (OR: 0.80; 95%CI: 0.70–0.93; p for interaction=0.89). There were 119 morphometric spine fractures over a maximum period of 4 years of follow-up (3 years in the vertebral fracture arm and 4 years in the clinical fracture arm). Overall, compared with placebo-treated women, alendronate reduced the risk of

spine fractures (OR: 0.54; 95% CI: 0.37–0.78). Treatment with alendronate reduced the risk of morphometric spine fractures to a similar degree in those with (OR: 0.72; 95% CI: 0.31–1.7) and without reduced renal function (OR: 0.50; 95% CI: 0.32–0.76; p for interaction=0.44). There was a small significant increase in serum creatinine from baseline to the 3-year follow-up (mean at baseline: 1.05 ± 0.16 versus mean at follow-up: 1.06 ± 0.16; p < 0.00001), but the increase in serum creatinine over the study period was the same in those with and without reduced renal function (mean increase in both groups: 0.01 ± 0.10;p=0.88) and was the same in both the placebo- and alendronate-treated groups (mean increase: 0.01 ± 0.10; p=0.99). Of the 6458 women in the study, 6426 reported an adverse event, but there was no difference in the frequency of reported events among women with reduced renal function (576 of 581 women or 99.1%) compared with women without reduced renal function (5850 of 5877 or 99.5%; p=0.189). More specifically, there was no difference in the frequency of gastrointestinal events (4.5% in women with reduced renal function compared with 5.2% among women without reduced renal function; p=0.5), cerebrovascular events (2.2% in both groups; p=0.9), cardiovascular events (2.6% in women with reduced renal function compared with 3.2; p=0.4), arrhythmias (2.4% in women with reduced renal function compared with 2.1; = 0.7), malignancies (4.3% in women with reduced renal function compared with 5.0 among women without reduced renal function; p=0.4), and death (1.6% in women with reduced renal function compared with 1.9; p=0.5). Furthermore, there was no difference in the frequency of renal adverse events in women with reduced renal function (12 of 581 or 2.1%) compared with those without (137 of 5877 or 2.3%; p=0.68).

In a study by Wetmore et al 31 healthy HD patients were randomized to placebo versus 40mg alendronate, taken once a week for 6 weeks. [70-92] Hip and lumbar spine BMD was measured by dual energy X-ray absorptiometry at baseline and at 6 months. Osteocalcin, parathyroid hormone, calcium, phosphorous and alkaline phosphatase levels were assayed at baseline and at 1, 3 and 6 months. Subjects ranged in age

from 41 to 82 years (mean 58±12 years); 22 (70%) were males and nine (30%) were females. Subjects were racially and ethnically diverse. The control subjects had higher BMD at Ward's Triangle at baseline. At Ward's Triangle of the hip, there was a loss of BMD in the control (placebo) group over the study duration (p=0.05) and a decrease in T-score as well (p=0.04), although not the Z-score. This trend was present but less pronounced, and not statistically significant, at the femoral neck and total hip. In contrast, BMD was stable at these sites in the treated group. Serum osteocalcin levels were measured at all time points for both groups. At baseline, there was no significant difference in the osteocalcin levels between groups. At 1 month, the treated group experienced a significant decrement in serum osteocalcin levels compared with the placebo group ($p< 0.05$). Osteocalcin levels remained depressed relative to baseline at 3 and 6 months within the alendronate-treated group; there was a trend toward increased osteocalcin in the placebo group. PTH was unchanged at 1, 3 and 6 months. There was no statistically significant difference in calcium, phosphorous or alkaline phosphatase levels at any time point in either group. No differences were observed at baseline or after 6 months between groups for any of the safety laboratory parameters evaluated (hematocrit, blood urea nitrogen, creatinine, potassium, albumin and AST; data not shown). Three subjects experienced gastric discomfort after the first dose, but tolerated subsequent doses without side effects. No patient had to be discontinued from the alendronate.

The study concluded that Low-dose alendronate, administered for a limited duration, appears to be well tolerated in dialysis patients. The BMD and T-scores declined at certain hip regions in the placebo group over 6 months, while remaining stable in the treatment group, suggesting a bone-preserving effect of alendronate.

Boonenet al[93] evaluated patients with GFR < 35 ml/min/1.73 m2 receiving zoledronic acid and did not describe worsening of renal function. It is noteworthy that all patients included in these studies had no evidence of CKD-MBD. In contrast, nephrotoxicity in patients receiving pamidronate or ibandronate were reported in a review.[94]

Intravenous bisphosphonates reduce fracture risk but have been associated in rare cases with deteriorating renal-function in cancer patients.

The renal effects of zoledronic acid were assessed in osteoporotic postmenopausal women from 27 countries who received three annual infusions of zoledronic acid or a placebo in a randomized, double-blind trial. [95] Serum creatinine, estimated creatinine clearance and urinary protein were measured before and after at least one infusion in a predefined renal safety cohort of 5035 equally divided patients. This group was compared to 7714 patients whose parameters were measured annually. Significantly more transient pre- to post-infusion increases in serum creatinine occurred in zoledronic acid than placebo-treated patients with significant elevations, relative to pre-infusion, only in the second year. All 31 zoledronic acid and 8 of 10 patients on placebo recovered their pre-infusion serum creatinine value within 12 months. No differences in mean changes in serum creatinine, estimated creatinine clearance or adverse renal events were found. The study found that transient changes in renal function can occur following an annual zoledronic acid infusion but, in the long term, renal function was not different from control patients. The intention-to-treat, safety, and renal safety populations comprised 7736, 7714, and 5035 patients, respectively. The renal safety population included 2521 patients in the zoledronic acid group and 2514 patients in the placebo group. Baseline demographic and disease-related characteristics for the safety population were similar for the two treatment groups. Patients in the renal safety cohort had similar baseline characteristics to the overall population. A total of 1219 patients (15.8%) discontinued the study. The rates of study discontinuation (zoledronic acid, 16.2%; placebo, 15.3%) and study discontinuation due to adverse events (zoledronic acid, 2.1%; placebo, 1.8%) were similar in the two treatment groups. Measurement of serum creatinine levels 9–11 days after each infusion showed that, overall, increases 40.5 mg/100 ml from the pre-infusion value occurred in 0.4% (10/2338) of placebo-treated patients and 1.3% (31/2320) of patients treated with 5mg of

zoledronic acid (P= 0.001;). Only 2/31 of the patients treated with 5mg of zoledronic acid had a change 40.5 mg/100 ml relative to their pre-infusion measurement at more than one time point. The incidence of increases by infusion with zoledronic acid 5 mg or placebo was 0.6 vs 0.3% (P=NS), 0.7 vs 0.1% (P = 0.002), and 0.5 vs 0.2% (P=NS) after infusions 1, 2, and 3, respectively. The percentage of patients experiencing an increase 40.5 mg/ 100ml from the pre-infusion value in the zoledronic acid group was greatest in those with baseline estimated creatinine clearance between 30 and 34 ml/min (10.6%) (more than four times greater incidence than the nearest baseline estimated creatinine clearance subgroup (35–39 ml/min). Increased serum creatinine levels returned to within 0.5mg/ 100ml of the pre-infusion value in all affected patients treated with 5mg of zoledronic acid (n = 31) and in 8 of the 10 affected placebo-treated patients within 12 months. For the 31 patients treated with 5mg of zoledronic acid, the mean serum creatinine levels at 9–11 days post-infusion and at 12 months post-infusion were similar after each infusion. The number of patients in whom urinary protein levels increased from a pre-infusion level p≤2+ to a level>2+ 9 to 11 days post-infusion was low. Overall, this occurred in 0.58% (13/2244) of patients treated with 5mg of zoledronic acid compared with 0.22% (5/2262) of the placebo group. (P=0.062). In patients treated with 5mg of zoledronic acid, the frequency of post-infusion urinary dipstick protein increases to >2+ was low after all infusions with a maximum incidence of 0.30% after infusion 2. No long-term differences in renal function were observed between the patients treated with 5mg of zoledronic acid and those treated by placebo. Mean changes from baseline in serum creatinine level (zoledronic acid, 0.1±0.14 mg/100 ml; placebo, 0.1±0.15 mg/100 ml) and estimated creatinine clearance (zoledronic acid, 8.8±9.58 ml/min; placebo, 8.7±9.62 ml/min) were almost identical in the two treatment groups over the 3 years of the study. Moreover, at month 36, 3.2% of patients in both groups had estimated creatinine clearance of 30 ml/min. Overall, at any time during the study, the incidence of renal abnormalities was similar between treatment groups. These included

reported renal adverse events (zoledronic acid, 4.9%; placebo, 4.4%), estimated creatinine. clearance < 30 ml/min (zoledronic acid, 4.4%; placebo, 4.2%; P=NS), estimated creatinine clearance decreases >30% in patients with baseline value < 60 ml/min (zoledronic acid, 5.0%; placebo, 4.8%; P=NS), and increased proteinuria (zoledronic acid, 0.5%; placebo, 0.5%; P=NS) (>2+in patients with baseline level ≤2+; zoledronic acid, 0.5%; placebo, 0.5%; P=NS). Increases from baseline in serum creatinine level >0.5mg/100ml were 2.8% with zoledronic acid and 2.0% with placebo (P=NS). Renal safety in patients with mild-to-moderate renal impairment Renal safety in patients with mild-to-moderate renal impairment was evaluated in patients with baseline estimated creatinine clearance between 30 and 60 ml/min. Overall, for zoledronic acid-treated patients, the incidence of an increase in serum creatinine > 0.5mg/100ml relative to baseline was similar in patients whose baseline estimated creatinine clearance was < 60 ml/min compared with those whose baseline estimated creatinine clearance was ≥ 60 ml/min (21 (1.99%) of 1053 patients vs 21 (1.66%) of 1267 patients, respectively;). Moreover, in the short term, no differences were observed in the incidence of an increase in serum creatinine > 0.5 mg/100 ml in patients with an estimated creatinine clearance of 35 to ≤ 60 ml/min and > 60 ml/min administered 5mg of zoledronic acid compared with placebo. In patients with an estimated creatinine clearance between 30 and 35 ml/min, five patients in the group treated with 5mg of zoledronic acid had an increase in serum creatinine > 0.5mg/100ml compared with one patient in the placebo group. The incidence of patients developing treatment-emergent estimated creatinine clearance <30 ml/min was greater for patients with a baseline calculated estimated creatinine clearance <40 ml/min in both treatment groups and is consistent with the average decline in renal function of the overall population-approximately 8 ml/min over 3 years. There was no relationship between the percentage change in creatinine clearance and baseline creatinine clearance. Acute renal failure (that is, serious adverse event requiring hospitalization) was reported in four patients treated with 5mg zoledronic acid (0.10%) and

in three placebo-treated patients (0.08%), based on an investigator's judgement of whether changes in creatinine clearance constituted an adverse event. That is, the determination of acute renal failure was subjective and was not based on any prespecified criteria, as evidenced by the fact that two of the four zoledronic acid-treated patients considered to have developed renal failure had baseline creatinine clearances of 31 ml/min and had only small changes below 30 ml/min. The overall incidence of reported renal failure was also similar between groups (zoledronic acid, 0.10%; placebo, 0.18%).

In another double-blind, placebo-controlled trial by Black et al.[95] 3889 patients (mean age, 73 years) were randomly assigned to receive a single 15-minute infusion of zoledronic acid (5mg) and 3876 were assigned to receive placebo at baseline, at 12 months, and at 24 months; the patients were followed until 36 months. Primary end points were new vertebral fracture (in patients not taking concomitant osteoporosis medications) and hip fracture (in all patients). Secondary end points included bone mineral density, bone turnover markers, and safety outcomes. Treatment with zoledronic acid reduced the risk of morphometric vertebral fracture by 70% during a 3-year period, as compared with placebo (3.3% in the zoledronic-acid group vs. 10.9% in the placebo group; relative risk, 0.30; 95% confidence interval [CI], 0.24 to 0.38) and reduced the risk of hip fracture by 41% (1.4% in the zoledronic-acid group vs. 2.5% in the placebo group; hazard ratio, 0.59; 95% CI, 0.42 to 0.83). Non vertebral fractures, clinical fractures, and clinical vertebral fractures were reduced by 25%, 33%, and 77%, respectively ($P<0.001$ for all comparisons). Zoledronic acid was also associated with a significant improvement in bone mineral density and bone metabolism markers. Adverse events, including change in renal function, were similar in the two study groups. However, serious atrial fibrillation occurred more frequently in the zoledronic acid group (in 50 vs. 20 patients, $P<0.001$).

Miller et al[96] have recently published a review of the literature on the renal safety of bisphosphonate use for osteoporosis. The authors concluded that the benefits outweigh risks; and even in elderly, frail,

osteoporotic patients with renal impairment, intravenous bisphosphonate therapy administration in accordance with the prescribing information did not result in long term renal function decline. One concern with bisphosphonate use in CKD patients is the induction of adynamic bone disease, due to the suppression of bone formation, resulting in bone fragility and fractures.

Amerling et al[97] studied 13 patients with CKD 2-4 in use of bisphosphonates through bone biopsy, and found that all of them developed adynamic bone disease. Thus, bisphosphonates are not indicated in patients with evidence of adynamic bone disease or osteomalacia.

Denosumab:

Denosumab (Dmab) The anti-RANKL monoclonal antibody decreases bone resorption and is useful for osteoporosis treatment and prevention of fractures in the general population. One advantage of this product compared to other osteoporosis drugs is that it does not have renal elimination.

Jamal et al[98] evaluated the effects of Dmab on fracture and BMD by level of kidney function in postmenopausal women included in FREEDOM study.

They examined the efficacy and safety of denosumab (DMAb) among subjects participating in the Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months (FREEDOM) Study. They estimated creatinine clearance (eGFR) using Cockcroft-Gault and classified levels of kidney function using the modified National Kidney Foundation classification of CKD. They examined incident fracture rates; changes in bone mineral density (BMD), serum calcium, and creatinine; and the incidence of adverse events after 36 months of follow-up in subjects receiving DMAb or placebo, stratified by level of kidney function. They used a subgroup interaction term to determine if there were differences in treatment effect by eGFR. Statistical analyses were performed on all patients randomized with baseline and at least one post baseline observation of interest (7393 subjects for new vertebral fracture, 7808 subjects for nonvertebral fracture, and 6363

subjects for lumbar spine BMD). By the CG, 73 women had stage 4 CKD; 2817 had stage 3, 4069 had stage 2 CKD, and the remaining 842 women had stage 1 CKD. By the MDRD, 17 women had stage 4 CKD, 1078 stage 3 CKD, 5413 had stage 2 CKD, and the remaining 1298 women had stage 1 CKD. None of these subjects had stage 5 CKD. Baseline characteristics were balanced between the treatment and placebo groups within each level of kidney function, and there were no substantial differences in the distribution of baseline variables using the MDRD compared with CG. Compared with women with stage 1 CKD, those with stage 4 CKD were older, weighed less, had poorer health status and physical function, and had lower BMD T-scores at the femoral neck and total hip. Overall, compared with placebo, denosumab reduced the incidence of new vertebral fractures [odds ratio (OR)= 0.30; 95% confidence interval (CI) 0.23–0.39) as well as the incidence of nonvertebral fractures over 36 months (OR= 0.78, 95% CI 0.66– 0.93). Denosumab was associated with an 8.8% (95% CI 8.6–9.1) increase in lumbar spine BMD, a 5.2% (95% CI 5.0–5.4) increase in femoral neck BMD, and a 6.4% (95% CI 6.3–6.5) increase in total hip BMD over 36 months. When they examined fracture risk, both vertebral and nonvertebral, by stage of CKD, by the CG, the treatment-by subgroup interaction term was not statistically significant, indicating that the reduction in fracture risk did not differ by level of kidney function. The incidence of vertebral fractures was lower among those randomized to DMAb compared with placebo for all stages of CKD but did not reach statistical significance among those with stage 4 CKD. Similarly the incidence of nonvertebral fractures was lower among those randomized to DMAb compared with placebo but was not statistically significant for stages 3 and 4 CKD. Owing to the small number of hip fractures (43 in the placebo group and 26 in the denosumab group), they did not examine differences in hip fractures by stage of CKD. Similarly, the treatment-by-subgroup interaction in BMD increase was not statistically significant, indicating that the increases in BMD did not differ by level of kidney function, and the magnitude of

increase in BMD was not substantially different Fracture risk reduction and changes in BMD at all sites were in favor of DMAb.

Block and cols[99] studied patients with GFR ranging from > 80 ml/min/1.73 m2 to kidney failure requiring hemodialysis, after a single-dose of D-mab. This 16-week study evaluated pharmacokinetics and pharmacodynamics of denosumab in 55 subjects with renal function ranging from normal to dialysis-dependent kidney failure. Participants received a single 60-mg subcutaneous dose of denosumab. Kidney function groups were based on calculations using the Cockcroft-Gault equation and U.S. Food and Drug Administration (FDA) guidance in place when the study was designed. Renal function did not have a significant effect on denosumab pharmacokinetics or pharmacodynamics. These findings suggest denosumab dose adjustment based on glomerular filtration rate is not required. Rapid decreases in serum C-telopeptide in all groups were sustained throughout the study. The most common adverse events were hypocalcemia (15%), pain in extremity (15%), and nausea (11%). Most adverse events were mild to moderate in severity. Calcium and vitamin D supplementation was not initially required by the study protocol, but was added during the trial. No subject who received adequate calcium and vitamin D supplementation became hypocalcemic. 8.0 mg/dL (<1.9 mmol/L and Seven subjects had nadir serum calcium concentrations between 7.5 and (<1.9 mmol/L). Two subjects (1symptomatic, 1asymptomatic) were hospitalized for intravenous calcium gluconate treatment. At the recommended dose, denosumab is a useful therapeutic option for patients with impaired renal function. Supplementation of calcium and vitamin D is strongly recommended when patients initiate denosumab therapy, particularly in patients with reduced renal function. The authors found no differences in pharmacokinetics and pharmacodynamics that justified dose adjustment based on GFR.

In another 6-month prospective, open-labeled study by Chen Liang et al[100] 12 patients on hemodialysis with low bone mass (T-score < −1.0 SD), were evaluated for effect of Denosumab on BMD. The BMD was

significantly increased in both the femoral neck (mean increase 23.7%±4.0%) and lumbar spine (17.1%± 2.6%) after 6 months of Denosumab.

Teriparatide:

This anabolic agent, analogue of PTH, is used to treat osteoporosis, especially in patients with severe disease and multiple fractures. In patients with mild to moderate CKD (GFR 30-79 mL/min/1.73 m2) who had normal serum PTH, teriparatide was effective in increasing BMD and reducing the risk of fractures, and also safe.[101]

Using data from the Fracture Prevention Trial, the safety and efficacy of teriparatide in postmenopausal women with osteoporosis and renal impairment were explored.[102] Patients were required to have serum creatinine concentrations < or =2.0 mg/dl and normal serum parathyroid hormone (PTH) concentrations and were randomized to receive daily subcutaneous injections of placebo or teriparatide 20 or 40 mcg/day. Glomerular filtration rate (GFR) was estimated using the Cockcroft-Gault equation. Patients were defined from baseline assessments to have normal (GFR > or =80 ml/min), mildly impaired (GFR 50-79 ml/min), or moderately impaired (GFR 30-49 ml/min) renal function for bone mineral density (BMD) and amino-terminal extension peptide of procollagen type 1 (PINP) analyses, and normal (GFR > or =80 ml/min) or impaired (GFR <80 ml/min) renal function for fracture analyses. Compared with patients with normal renal function, patients with renal impairment were older, shorter, weighed less, had been postmenopausal longer, and had lower baseline lumbar spine and femoral neck BMD. Compared with placebo, teriparatide significantly increased PINP and lumbar spine and femoral neck BMD within each renal function subgroup, and there was no evidence that these increases were altered by renal insufficiency (each treatment-by-subgroup interaction p>0.05). Similarly, teriparatide-mediated vertebral and nonvertebral fracture risk reductions were similar and did not differ significantly between patients with normal or impaired renal function (treatment-by-subgroup interactions p>0.05). The incidences of treatment-emergent and renal-related adverse events were consistent

across treatment assignment in the normal, mildly impaired, and moderately impaired renal function subgroups. Teriparatide induced changes in mean GFR were unaffected by baseline renal function (treatment-by-renal function interaction p>0.05 for normal, mildly impaired, or moderately impaired subgroups). Patients in all renal function categories treated with teriparatide 20 or 40 mcg had an increased incidence of 4-6-h post dose serum calcium >10.6 mg/dl (the upper limit of normal) versus placebo; however, teriparatide 20 mcg/day was not associated with significantly increased incidence of 4-6-h post dose serum calcium >11 mg/dl in any renal function category. Teriparatide therapy was associated with increased incidence of elevated uric acid, with the incidences being highest in patients with moderately impaired renal function and in those receiving teriparatide 40 mcg/day. Even so, adverse event data did not suggest an increased incidence of gout or arthralgia or of nephrolithiasis events in teriparatide-treated patients with normal, mild, or moderate renal impairment.

As increased PTH levels constitutes a contraindication to teriparatide[20], the use of this drug in CKD, a condition related to hyperparathyroidism, seems inappropriate. Teriparatide might be useful in CKD patients with adynamic bone disease, where hyperparathyroidism is not the central disorder, and in those who underwent prior parathyroidectomy, but few studies have evaluated its use in these conditions.[8,20]

Selective estrogen receptor modulators (SERM)

Selective estrogen receptor modulators was evaluated by Ishani and cols.[103] in patients with mild to moderate CKD. The data from a multicenter, randomized, placebo-controlled trial of 7705 postmenopausal women with osteoporosis, the effect of raloxifene on rate of change of bone mineral density (BMD), incidence of fractures, and adverse events by stage of CKD was examined over 3 yr. Baseline serum creatinine values were available for 7316 women, and these values were used to assign a category of creatinine clearance (CrCl) using the Cockcroft-Gault formula (CrCl <45, 45 to 59, and >60ml/min).

BMD was measured at baseline and annually by dual x-ray absorptiometry. Within each category of kidney function, adverse events were similar between the raloxifene and placebo groups. In conclusion, raloxifene increases BMD at both the hip and the spine and reduces the risk for vertebral fractures among individuals with CKD. The effect of raloxifene on hip BMD is greater among those with mild to moderate CKD. Of the 7316 women in this analysis cohort, 5675 (78%) completed technically adequate BMD measurements at baseline and 3 yr. There was evidence of an interaction between baseline category of CrCl and treatment assignment for prediction of rate of change in BMD at the hip (p=0.005 for interaction term at the femoral neck and 0.01 at the trochanter). Consequently, all additional analyses performed for change in BMD at either the femoral neck or the trochanter were stratified by treatment assignment. Within the placebo group, lower CrCl seemed to be associated with higher annual losses of BMD at the femoral neck, but the trend did not reach significance (p=0.09 for trend); however, within the raloxifene group, the trend was in the opposite direction, in that the effect of raloxifene in increasing femoral neck BMD was most pronounced among women with lower CrCl (*P* =0.01 for trend). Compared with placebo, the effect of raloxifene on increasing femoral neck BMD was 1.0% per year among women with a CrCl <45 ml/min, 0.7% per year among women with a CrCl of 45 to 59 ml/min, and 0.6% per year among women with a CrCl >60 ml/min (p<0.001 for all comparisons between pooled raloxifene treatment group and placebo group). Substitution of trochanteric BMD for femoral neck BMD or the absolute rate of change in BMD for percentage change in BMD did not alter the results. When using the MDRD eGFR in place of the Cockcroft-Gault CrCl, there was no evidence of an interaction between category of kidney function and annualized percentage change in BMD at either the femoral neck (p=0.44 for interaction) or the trochanter (p=0.35 for interaction); however, the overall effect on hip BMD was similar, with women in the pooled raloxifene treatment group gaining hip BMD over 3 yr, whereas those in the placebo group experienced losses in hip BMD, irrespective of

category of eGFR. Unlike at the femoral neck, the effect of raloxifene on rate of change in spine BMD did not differ by category of CrCl atbaseline (p =0.54 for interaction). In general, lower CrCl was associated with greater increases in spine BMD irrespective of treatment assignment (p=0.006 for trend within placebo group and *P* <0.001 within pooled raloxifene group. Results were similar when eGFR was substituted in place of the CrCl (p=0.98 for interaction). Irrespective of kidney function, raloxifene treatment was associated with reduction in vertebral fractures, and no effect on nonvertebral fractures compared with placebo. Within each category of kidney function, adverse events were similar between the raloxifene and placebo groups. It was concluded that raloxifene increases BMD at both the hip and the spine and reduces the risk for vertebral fractures among individuals with CKD. The effect of raloxifene on hip BMD is greater among those with mild to moderate CKD.

Raloxifene is commonly used for treatment of postmenopausal osteoporosis in the general population, and use of raloxifene for hemodialysis patients has also been reported. Raloxifene is likely to be an expectant treatment option for osteoporosis in hemodialysis patients. It increased BMD and reduced the risk of vertebral fractures. There were no significant side effects, although an increase in raloxifene plasma levels in CKD patients has been published[104] One concern is the increased risk of stroke[105] and fatal deep vein thrombosis, which limits its use in patients with increased risk of thromboembolic and cardiovascular diseases as seen in CKD.

Bazedoxifene, another SERM approved for osteoporosis treatment, has also been evaluated in patients with mild to moderate renal impairment. It reduced the risk of fractures and was safe.[106]

Two global, double-blind, placebo- and active-controlled, phase-3 studies (2-year prevention (n =1583) and 3-year treatment (n =7492)) have shown that bazedoxifene (BZA) is safe and effective for prevention and treatment of postmenopausal osteoporosis. Data for the BZA 20- and 40-mg and placebo groups from both studies were integrated for assessment of bone turnover markers (BTMs), bone

mineral density (BMD), and fracture incidence (treatment study only). Safety was assessed using integrated data for the BZA, placebo, and raloxifene 60-mg groups from both studies. Baseline glomerular filtration rate (GFR) was estimated by the Modification of Diet in Renal Disease Study equation; among subjects with baseline GFR, renal function categories were defined by GFR (ml/min per 1.73 m^2): normal (GFR ≥ 90; n=1982), mild impairment (GFR ≥ 60 to < 90; n=6032), or moderate/severe impairment (GFR < 60; n=723).

Demographics were similar across treatment groups and within GFR subgroups. Across GFR subgroups, BZA 20 and 40 mg reduced BTM levels and improved lumbar spine and total hip BMD versus placebo. At month 24, there were significant treatment-by-GFR (p =0.003) and treatment-by-serum creatinine (p=0.034) interactions for the increase in lumbar spine BMD versus placebo. Fracture incidence was lower with BZA than placebo across all GFR categories, with no treatment-by-GFR interaction. There were no significant differences among treatment groups in incidences of overall, serious, or renal-related adverse events across GFR subgroups. It was concluded that Mild to moderate kidney impairment did not affect the efficacy and safety of BZA in postmenopausal women.

Tanaka et. al[107] evaluated the efficacy of raloxifene and its effects on bone mineral metabolism in postmenopausal Japanese patients on dialysis. In addition to renal osteodystrophy, postmenopausal women on hemodialysis are at high risk for osteoporosis. In a prospective, multicentre study, 17 postmenopausal women on chronic hemodialysis with severe osteoporosis (bone mineral density [BMD] <2 SD by bone densitometry) were treated with 60 mg/day raloxifene hydrochloride for 12 months. The study also included 10 age-matched control women. Vitamin D and calcium salts were not changed during the study. Intact parathyroid hormone (iPTH), serum calcium and phosphorus, and bone resorption marker (NTx) were measured, and BMD were determined by DEXA, at 0, 6, and 12 months after administration of raloxifene. The mean lumbar spine BMD at baseline was similar in the two groups. Raloxifene therapy (for 12 months) improved lumbar spine BMD (by

2.6%) in 53% of the patients, while 70% of the control group showed a reduction in BMD (by 4.0%). Raloxifene significantly decreased serum calcium and increased iPTH. Their results suggested that raloxifene improved trabecular BMD in postmenopausal Japanese women on hemodialysis. The effects of raloxifeneon serum calcium and serum iPTH level suggest it improves bone resorption. Vitamin D and/or calcium salts should be added to raloxifene treatment to avoid secondary hyperparathyroidism.

Calcitonin

The calcium sparing effect of calcitonin in renal tubules might decrease PTH in CKD, a condition associated with hyperparathyroidism. However, tachyphylaxis with prolonged use and lack of efficacy in non-vertebral fractures, as well as the paucity of data in CKD patients do not favor its use in CKD.

MATERIAL AND METHODS

The prospective case control study was done on patients with CKD stage 3-5D, presenting to Nephrology ward, OPD of department of Nephrology and/or dialysis unit, of Dayanand Medical College and Hospital, Ludhiana. The study was cleared by the institute ethical committee and approved by the State Medical University (Baba Farid University of Health Sciences, Faridkot). The study period was from Feb 2018 to July 2019.

INCLUSION CRITERIA

Patients between the age of 18 to 70 yrs with CKD3-5D with informed consent were included.

EXCLUSION CRITERIA

1. Patients who refused to give consent
2. Patients with age < 18 and >70 year
3. Renal transplant recipients
4. H/O of previous use antiresorptive therapy in last 6 months
5. Patients on steroids or h/o steroid intake in past.
6. Females patients who have taken any hormone replacement therapy or SERM like raloxifine in past 12 months.
7. Patients with severe chronic co-morbidity like CLD, COPD, bronchial asthma and malignancy, etc.
8. Patient with adynamic bone disease (with PTH < 130 and/or bone specific alkaline phosphatease < 30)

METHODS OF COLLECTION OF DATA

After an informed consent, relevant history taking and physical examination was done. A predefined proforma was used to collect the whole data including relevant investigations related to CKD and BMD, which included:

Complete blood counts

ESR

Serum creatinine, urea & electrolytes,

Serum calcium and phosphorus

Serum alkaline phosphatase

Uric acid

Liver function tests

Vitamin D3 levels

PTH levels and/or bone specific alkaline phosphatase

Urine routine examination

USG KUB.

X ray Dorso-lumbar spine lateral view and X ray hands

Chest X ray

Echocardiography (if required)

DEXA scan - At level of lumbar spine (L1-L4), femoral neck and total hip was done to measure BMD with T score and age matched Z score as per WHO'scriteria:

T score at or above -1 SD, defined as normal

T score between -1 to -2.5 SD defined as osteopenia

T score at or below -2.5 SD. defined as osteoporosis

GFR was calculated as per The CKD-EPI equation, as currently recommended by the international consensus KDIGO 2012 guidelines.

Patients of CKD were staged into following categories.

Categories	GFR (ml/min/1.73 m2)
G1	≥ 90 Normal or high
G2	60-89 Mildly decreased
G3a	45-59 Mildly to moderately decreased
G3b	30-44 Moderately to severely decreased
G4	15-29 Severely decreased
G5	< 15 Renal failure

Patients were initially screened by above mentioned investigations. All the patients with T score < -1 SD on DEXA scan, meeting inclusion criteria were enrolled for the study.

Out of total 80 patients selected for final analysis, there was further subdivision into two sub groups; one group was of 40 Patients of CKD stage 3-5D, who received Antiresorptive therapy in form of oral alendronate along with vitamin D3. This group was compared another group of 40 patients of CKD stage 3-5D who did not receive oral alendronate and served as controls. Patients in case group were given

35 mg of alendronate once weekly i.e. 70 mg half tablet with glass of water on empty stomach in morning and were advised not to lie down for an hour after drug intake. Patients were followed till one year with all these repeat investigations till completion of study.

Outcomes:

Primary outcomes:

Primary outcomes of study were assessed with help of DEXA scan and X rays and biochemical parameters.

DEXA scan: This was done at baseline and was repeated at 6 month and 12 month to assess the effect of antiresorptive therapy on the status of BMD.

X RAYS: X ray Dorso-lumbar spine and X ray hands were repeated at 6 month and 12 months to look for evidence of any fractures and vascular calcification.

Secondary outcomes:

Secondary out comes were assessed by looking for adverse reactions related to treatment during each follow up visits.

Patients were also assessed for improvement in biochemical parameters including calcium, phosphorus, vitamin D3 and iPTH level.

STATISTICAL ANALYSIS

Data were described in terms of range; mean ± standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. For comparing categorical data, Chi square ($\chi 2$) test were used. T test was used for comparison between test and control groups. A probability value (p value) less than 0.05 was considered statistically significant. ANOVA was also used in this study. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 17 version statistical program for Microsoft Windows.

OBSERVATIONS AND RESULTS

The prospective case control study was done in patients with CKD stage 3-5D.The study period was from Feb 2018 to July 2019. A total of 80 patients finally completed the study period duration and were included in final analysis.

TABLE 1: GENDER WISE DISTRIBUTION OF THE PATIENTS

						Total
		Control		Case		
Sex	F	13	32.5%	10	25.0%	23
	M	27	67.5%	30	75.0%	57

23 patients (32.5%) were female and 57 patients (67.5%) were male, thus giving a male to female ratio of 2.4:1.

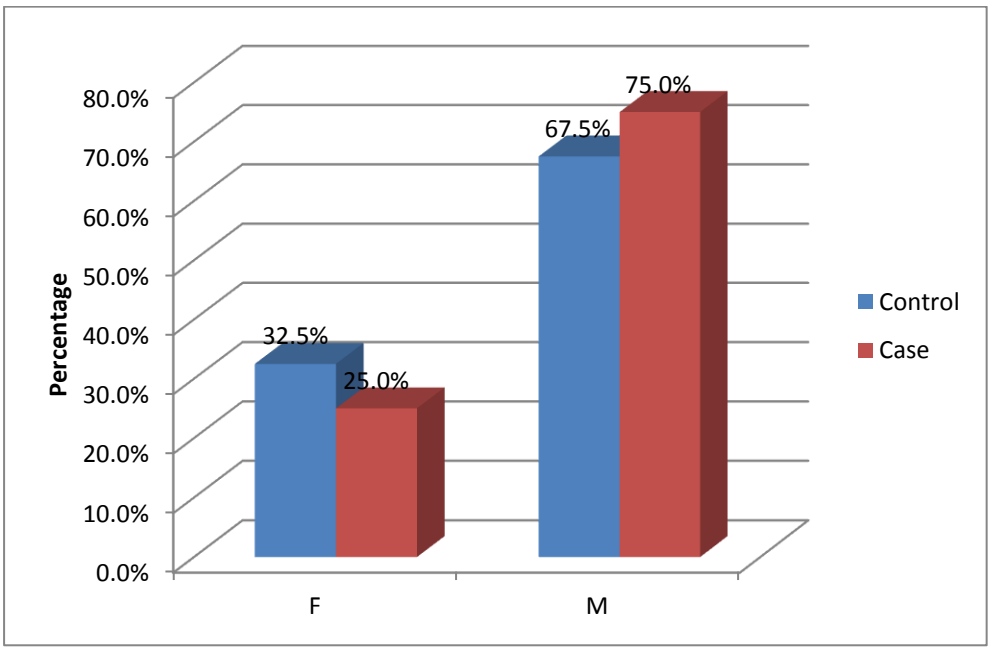


FIGURE 1: GENDER WISE DISTRIBUTION OF THE PATIENTS

TABLE 2: AGE DISTRIBUTION OF THE PATIENTS

						Total
		Control		Case		
Age group	<40	6	15.0%	4	10.0%	10
	41-50	7	17.5%	6	15.0%	13
	51-60	13	32.5%	15	37.5%	28
	>60	14	35.0%	15	37.5%	29

57 (67.5%) of patients were in age group older than 50. Only 10 (12.5%) were younger than age of 40. Both cases and controls were comparable in age distribution.

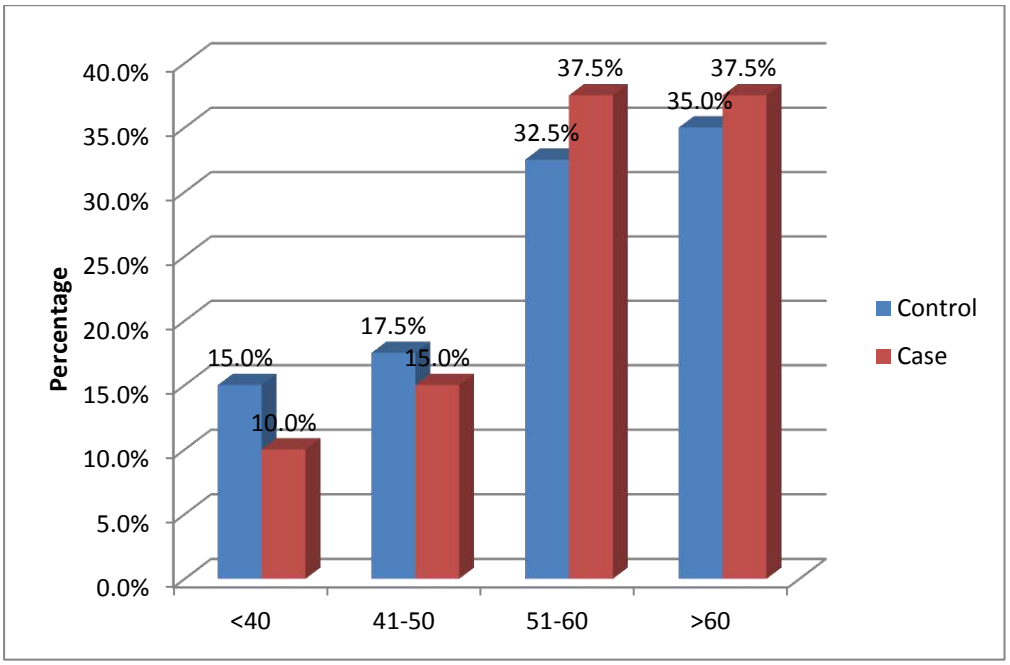


FIGURE 2: AGE DISTRIBUTION OF THE PATIENTS

TABLE 3: DISTRIBUTION ACCORDING TO RESIDENTIAL STATUS

						Total
		Control		Case		
Address	rural	12	30.0%	7	17.5%	19
	urban	28	70.0%	33	82.5%	61

19 patients were from rural and 61 were urban background respectively. There was no difference between case or control group.

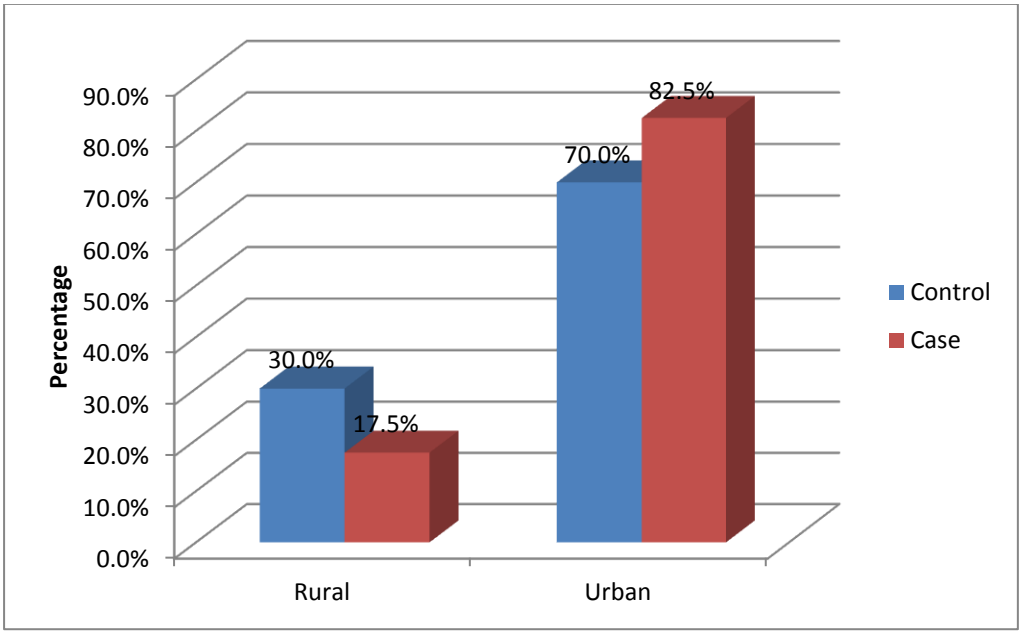


FIGURE 3: DISTRIBUTION ACCORDING TO RESIDENTIAL STATUS

TABLE 4: DISTRIBUTION ACCORDING TO CKD STAGE

						Total
		Control		Case		
CKD stage	3	7	17.5%	7	17.5%	14
	4	6	15.0%	6	15.0%	12
	5	7	17.5%	7	17.5%	14
	5D	20	50.0%	20	50.0%	40

A total of 14 (17.5%), 12 (15%), and 14 (17.5%) were in CKD stage 3, 4 and 5 respectively. 40 (50%) patients had CKD 5D stage.

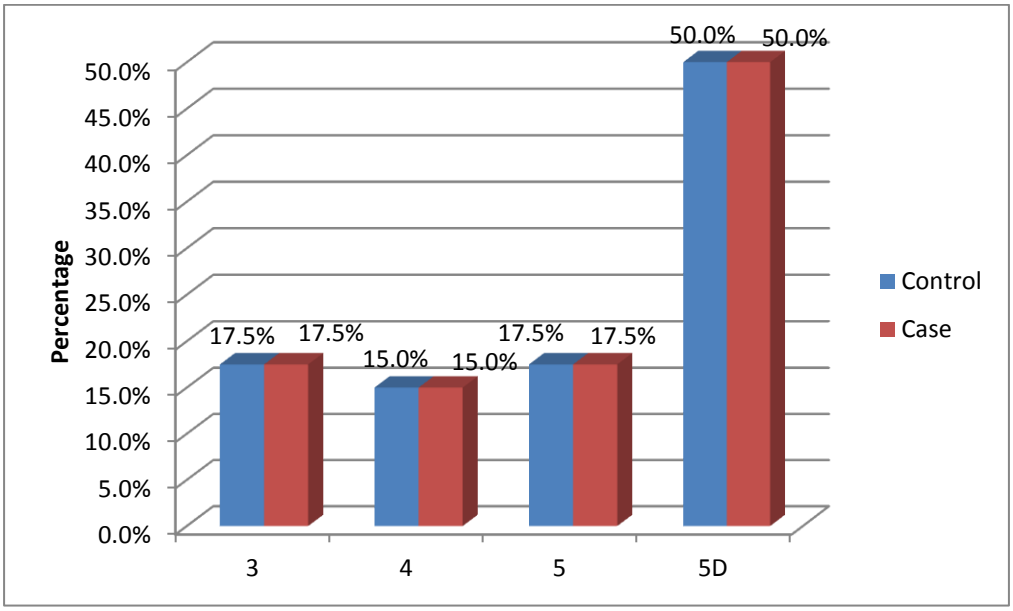
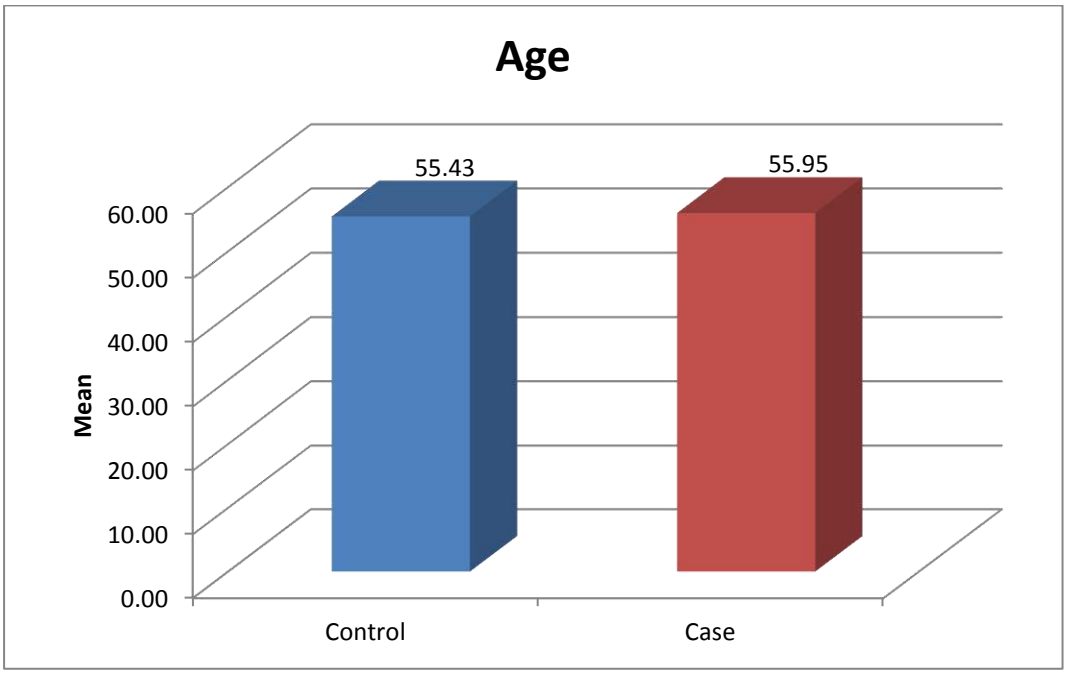


FIGURE 4: DISTRIBUTION ACCORDING TO CKD STAGE

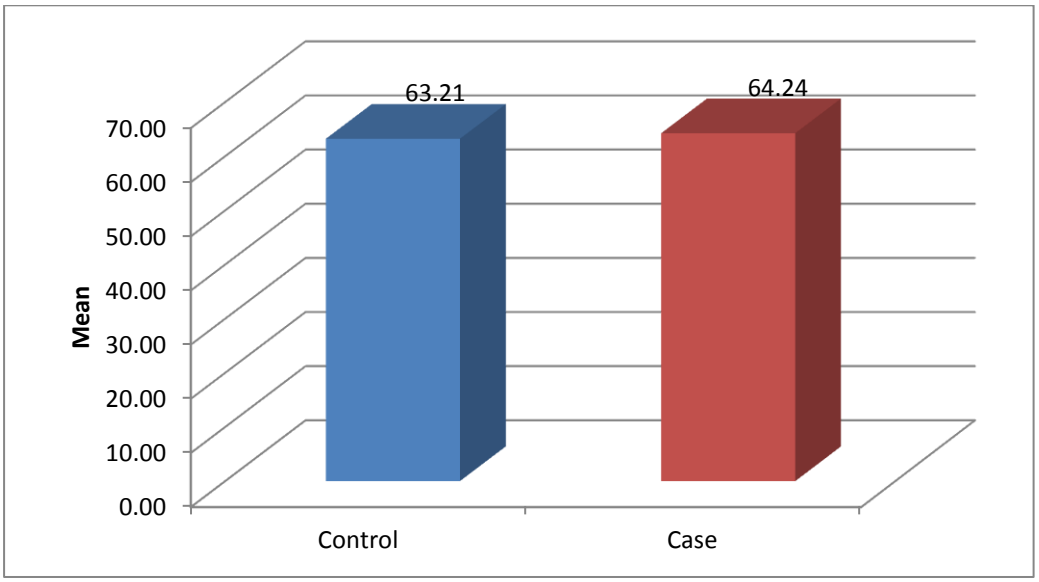
TABLE 5: COMPARISON OF BASELINE DEMOGRAPHIC FEATURES

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Age	55.43	11.17	55.95	9.88	-0.223	0.824	-0.53	2.36
Weight in Kg	63.21	8.50	64.24	11.00	-0.467	0.641	-1.03	2.20
Height in cm	165.95	4.18	167.43	2.96	-1.821	0.072	-1.48	0.81
SBP	128.85	6.45	129.30	9.56	-0.247	0.806	-0.45	1.82
DBP	81.70	4.85	81.45	5.14	0.224	0.824	0.25	1.12

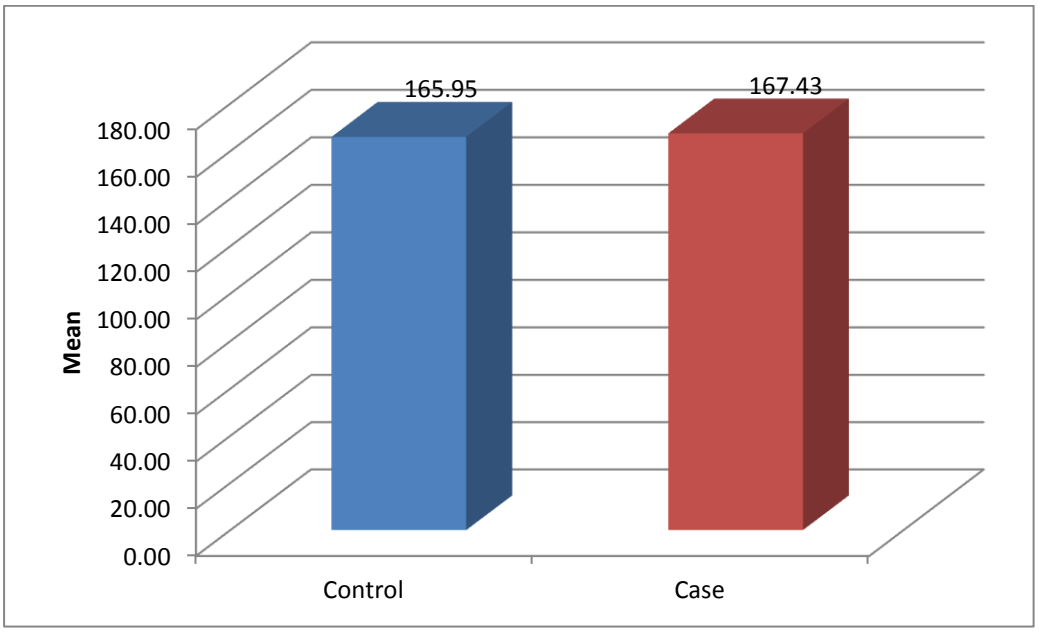
Mean age of control and case group was 55.43 (SD=11.17) and 55.95 (SD=9.88) respectively. There was no statistically significant difference between two groups.



Mean weight of control and case group was 63.21(SD=8.50) and 64.24(SD=11.0) respectively. There was no statistically significant difference between two groups.



Mean height of control and case group was 165.95(SD=4.18) and 167.43 (SD=2.96) respectively. There was no statistically significant difference between two groups.



Mean SBP for control and case group was 128.85 (SD= 6.45) and 129.30 (SD= 9.56) respectively. Mean DBP for control and case group was 81.70 (SD= 4.85) and 81.45 (SD= 5.14) respectively.

FIGURE 5: COMPARISON OF BASELINE DEMOGRAPHIC FEATURES

TABLE 6: COMPARISON OF CARDIAC COMORBIDITIES

						Total
		Control		Case		
Cardiac comorbidity	LVEF 30-40%	2	5.0%	3	7.5%	5
	LVEF>40%	3	7.5%	3	7.5%	6

5 patients in control and 6 patients in case group had underlying DCMP. 2 patients in control and 3 in case group had LVEF between 30-40%.

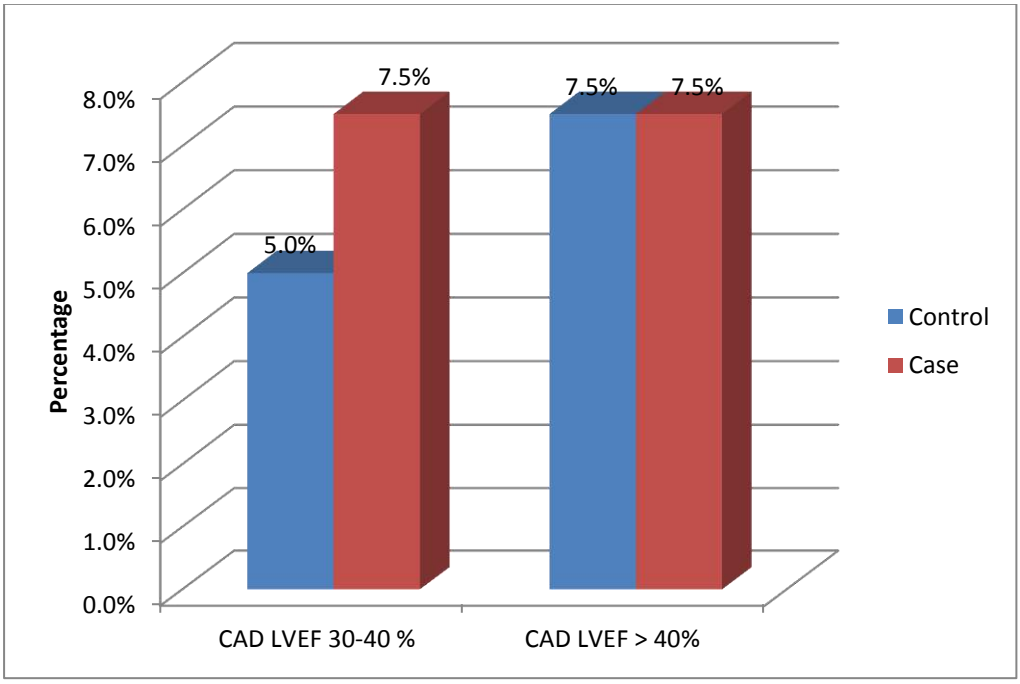


FIGURE 6: COMPARISON OF CARDIAC COMORBIDITIES

TABLE 7: COMPARISON OF BASELINE COMPLETE BLOOD COUNTS

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Hemoglobin baseline g/dl	9.43	0.60	9.37	0.67	0.458	0.648	0.07	0.14
TLC baseline per ul	8.34	1.60	8.62	1.58	-0.774	0.441	-0.27	0.36
Platelets at baseline lakh	1.51	0.25	1.61	0.35	-1.511	0.135	-0.10	0.07

Baseline mean hemoglobin was 9.43 (SD= 0.60) and 9.37(SD= 0.67) for control and case group respectively. Baseline TLC was 8.34 (SD=1.60) and 8.62 (SD=1.58) for control and case group respectively. Baseline platelet count was 1.51 (SD=0.25) and 1.61 (SD=0.35) for control and case group respectively.

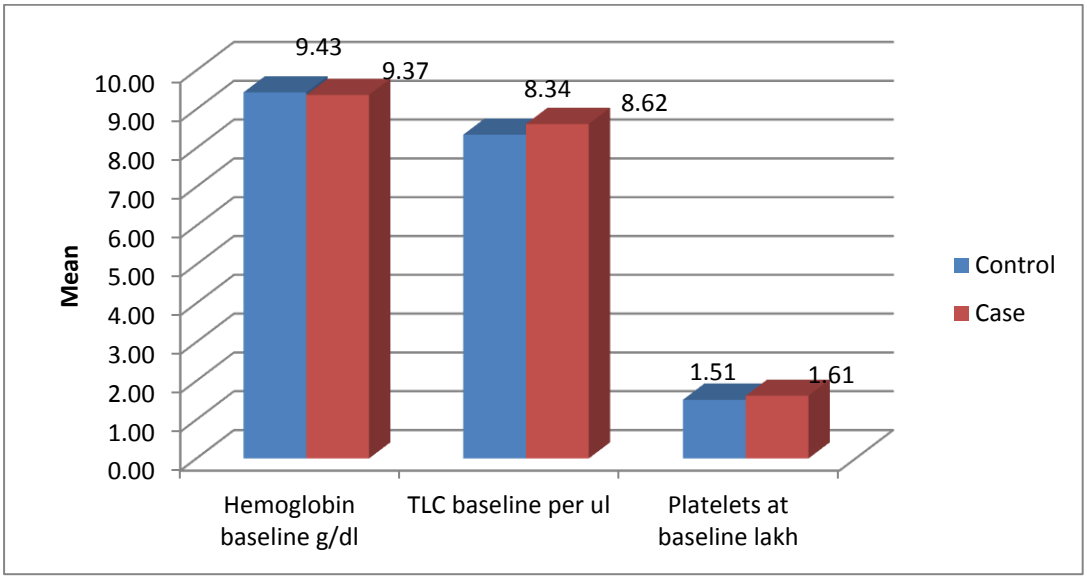
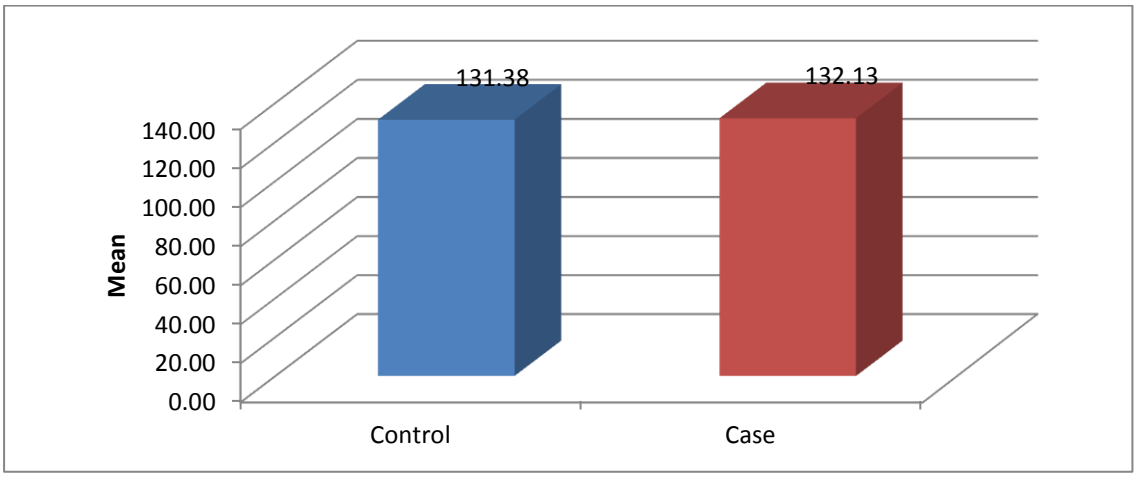


FIGURE 7: COMPARISON OF BASELINE COMPLETE BLOOD COUNTS

TABLE 8: COMPARISON OF THE MEAN UREA AND CREATININE AT BASELINE

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Urea at baseline mg/dl	131.38	14.74	132.13	16.57	-0.214	0.831	-0.75	3.51
Creatinine baseline mg/dl	3.99	1.24	4.15	1.32	-0.541	0.590	-0.16	0.29

Baseline mean urea was 131.38 (SD= 14.74) and 9.37 (SD= 16.57) for control and case group respectively. Baseline mean creatinine was 3.99 (SD= 1.24) and 4.15 (SD= 1.32) for control and case group respectively.



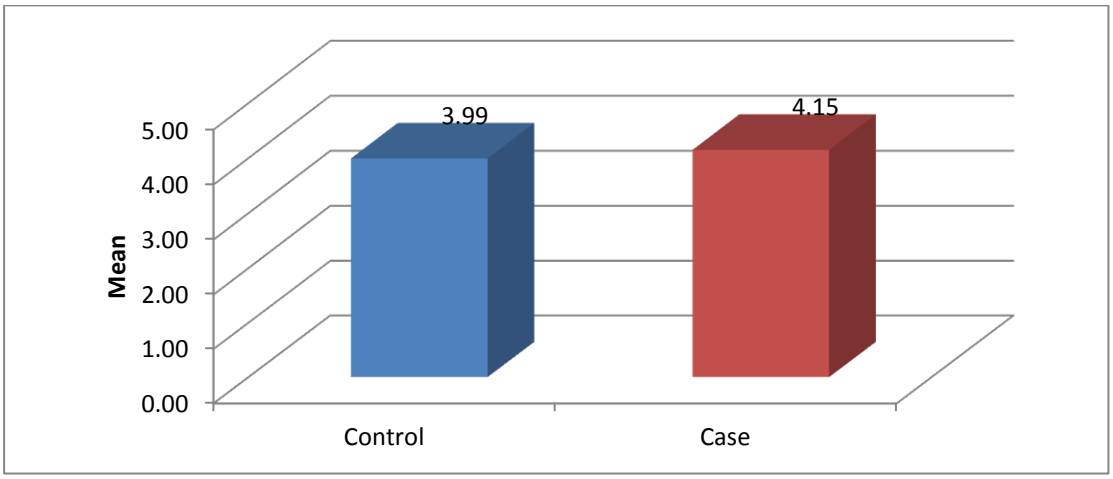


FIGURE 8. COMPARISON OF THE MEAN UREA AND CREATININEAT BASELINE

TABLE 9: COMPARISON OF THE MEAN SODIUM AND POTASSIUM AT BASELINE

	control		case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Sodium baseline meq/l	135.65	5.25	135.75	7.29	-0.070	0.944	-0.10	1.42
Potassium at baseline meq/l	4.40	1.02	4.51	1.05	-0.464	0.644	-0.11	0.23

Baseline mean sodium was 135.65(SD= 5.25) and135.75 (SD= 7.29) for control and case group respectively. Baseline mean potassium was 4.40 (SD= 1.02) and 4.51(SD= 1.05) for control and case group respectively.

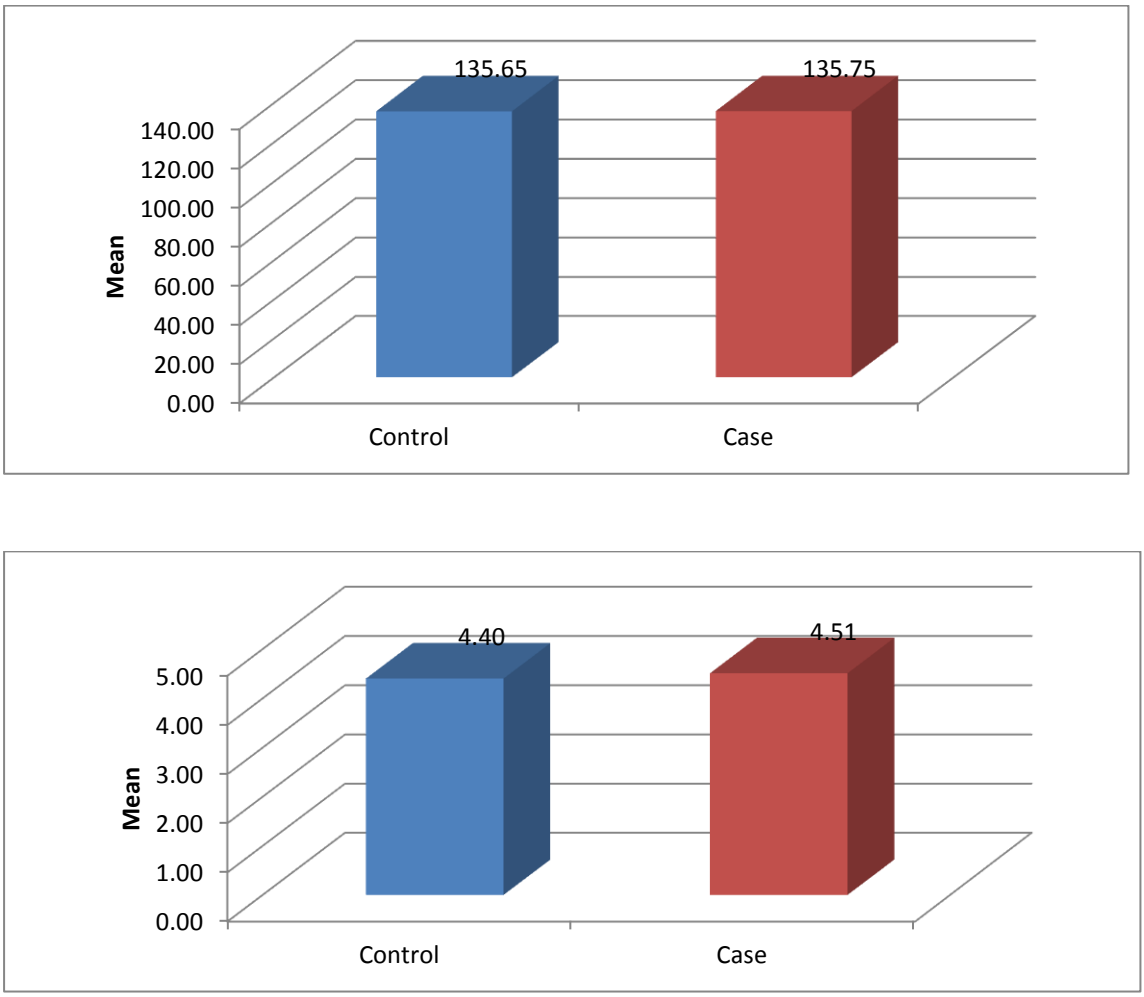


FIGURE 9: COMPARISON OF THE MEAN SODIUM AND POTASSIUM AT BASELINE

TABLE 10: COMPARISON OF THE MEAN CREATININE

	control		case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Creatinine baseline mg/dl	3.99	1.24	4.15	1.32	-0.541	0.590	-0.16	0.29
Creatinine at 3 months	4.47	1.41	4.28	1.53	0.586	0.560	0.19	0.33
Creatinine at 6 months	4.60	1.46	4.36	1.48	0.714	0.477	0.23	0.33
Creatinine at 12 months	4.65	1.45	4.72	1.56	-0.223	0.824	-0.08	0.34

Mean creatinine values were 3.99 (SD=1.24), 4.47 (SD=1.41), 4.60 (SD=1.46) and 4.65 (1.45) at baseline, 3 months, 6months and 12 months respectively in control group. Mean creatinine values were 4.15 (SD=1.32), 4.28(SD=1.53), 4.36(SD=1.48) and 4.72 (1.56) at baseline, 3 months, 6months and 12 months respectively in case group.

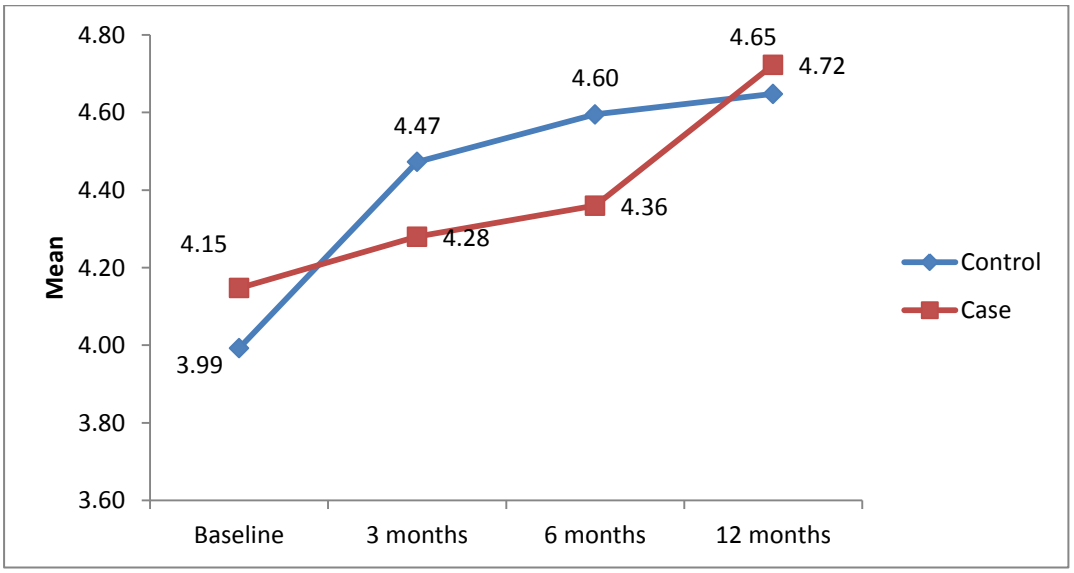


FIGURE 10: COMPARISON OF THE MEAN CREATININE

TABLE 11: COMPARISON BETWEEN DIFFERENCES OF MEAN CREATININE

Overall	control		case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-3m	-0.48	1.23	-0.13	1.16	-1.298	0.198	-0.35	0.27
0- 6m	-0.60	1.32	-0.21	1.37	-1.298	0.198	-0.39	0.30
0-12m	-0.66	1.25	-0.58	1.08	-0.306	0.761	-0.08	0.26
3-6m	-0.12	1.08	-0.08	1.17	-0.169	0.867	-0.04	0.25
3-12m	-0.18	1.59	-0.44	1.48	0.778	0.439	0.27	0.34
6-12m	-0.05	1.34	-0.36	1.18	1.100	0.275	0.31	0.28

There was statistically no difference in change in the mean value of creatinine at 3, 6 and 12 months between control and case group. This was -0.48, -0.60, -0.66 at 3, 6 and 12 months for controls. This was -0.13, -0.21, -0.58 at 3, 6 and 12 months for cases.

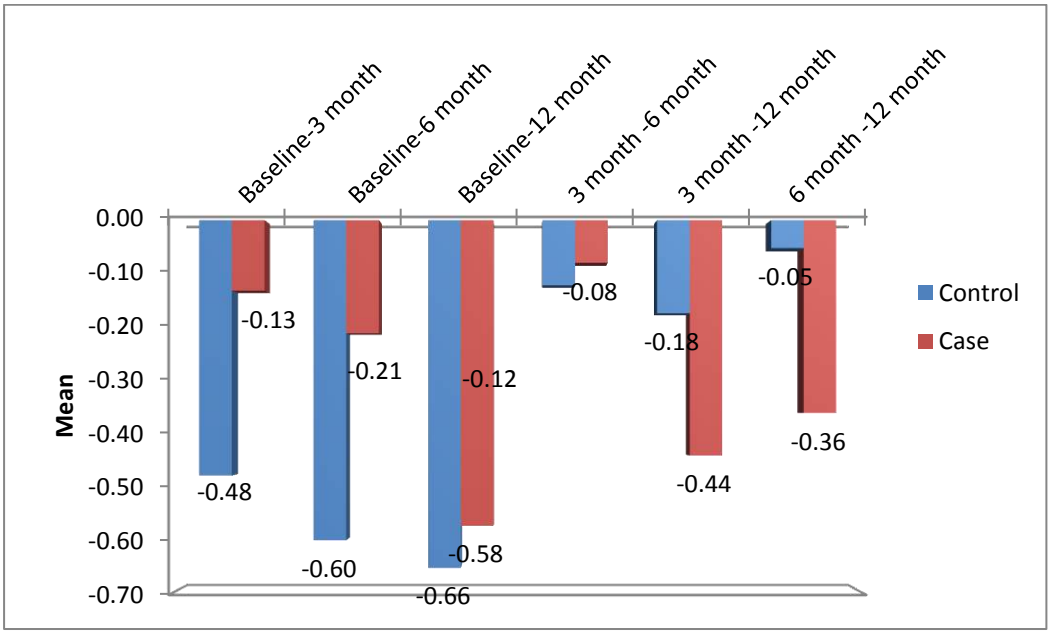


FIGURE 11: COMPARISON BETWEEN DIFFERENCES OF MEAN CREATININE

TABLE 12: COMPARISON OF THE MEAN SERUM CALCIUM VALUE

Overall	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Calcium baseline mg/dl	8.62	0.60	8.57	0.61	0.425	0.672	0.06	0.14
Calcium at 3 months	8.49	0.58	8.61	0.57	-0.916	0.363	-0.12	0.13
Calcium at 6 months	8.54	0.53	8.57	0.72	-0.213	0.832	-0.03	0.14
Calcium at 12 months	8.61	0.72	8.43	0.63	1.201	0.233	0.18	0.15

There was no difference in mean calcium level at baseline, 3, 6 and 12 months between control and case group. This was 8.62, 8.49, 8.54, 8.61 at baseline, 3, 6 and 12 months for controls. This was 8.57, 8.61, 8.57, 8.43 at baseline, 3, 6 and 12 months for cases.

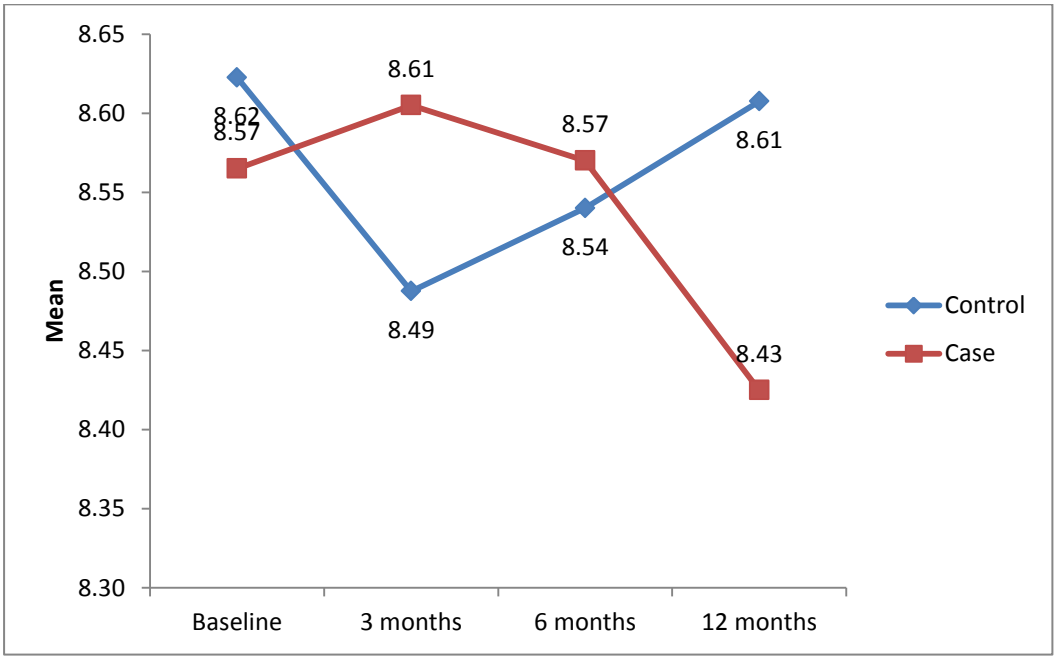


FIGURE 12: COMPARISON OF THE MEAN SERUM CALCIUM VALUE

TABLE 13: COMPARISON OF THE MEAN SERUM PHOSPHORUS VALUE

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Phosphorus baseline	6.76	1.34	6.56	1.20	0.702	0.485	0.20	0.28
Phosphorus at 3 months	6.41	0.68	6.61	0.83	-1.176	0.243	-0.20	0.17
Phosphorus at 6 months	6.64	1.09	6.69	1.02	-0.223	0.824	-0.05	0.24
Phosphorus at 12 months	6.79	1.23	6.62	0.94	0.717	0.476	0.18	0.24

There was no difference in mean phosphorus level at baseline, 3, 6 and 12 months between control and case group. This was 6.76, 6.41, 6.64, 6.79 at baseline, 3, 6 and 12 months for controls. This was 6.56, 6.61, 6.69, 6.62 at baseline, 3, 6 and 12 months for cases.

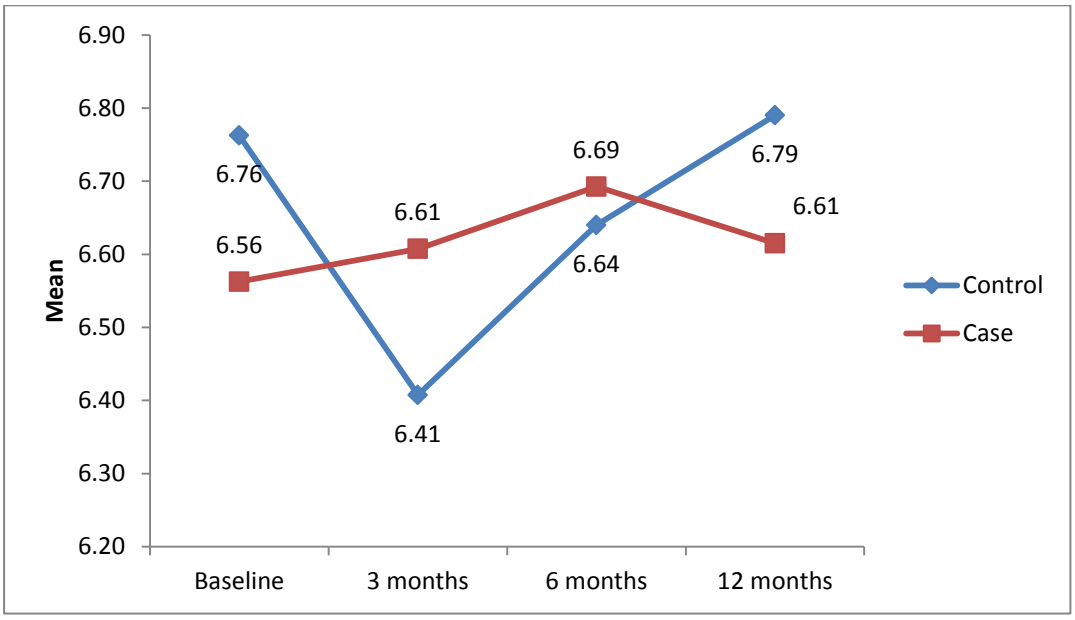


FIGURE 13: COMPARISON OF THE MEAN SERUM PHOSPHORUS VALUE

TABLE 14: COMPARISON OF THE MEAN SERUM ALKALINE PHOSPHATASE VALUE

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Base line U/dl	150.10	12.70	146.45	11.43	1.351	0.181	3.65	2.70
3 month	145.33	10.82	149.93	14.83	-1.585	0.117	-4.60	2.90
6 month	148.00	11.74	148.50	12.84	-0.182	0.856	-0.50	2.75
12 month	145.40	9.17	141.63	14.50	1.392	0.168	3.78	2.71

There was no difference in mean ALP level at baseline, 3, 6 and 12 months between control and case group. This was 150.10, 145.33, 148.00, 145.40 at baseline, 3, 6 and 12 months for controls. This was 146.45, 149.93, 148.50, 141.63 at baseline, 3, 6 and 12 months for cases.

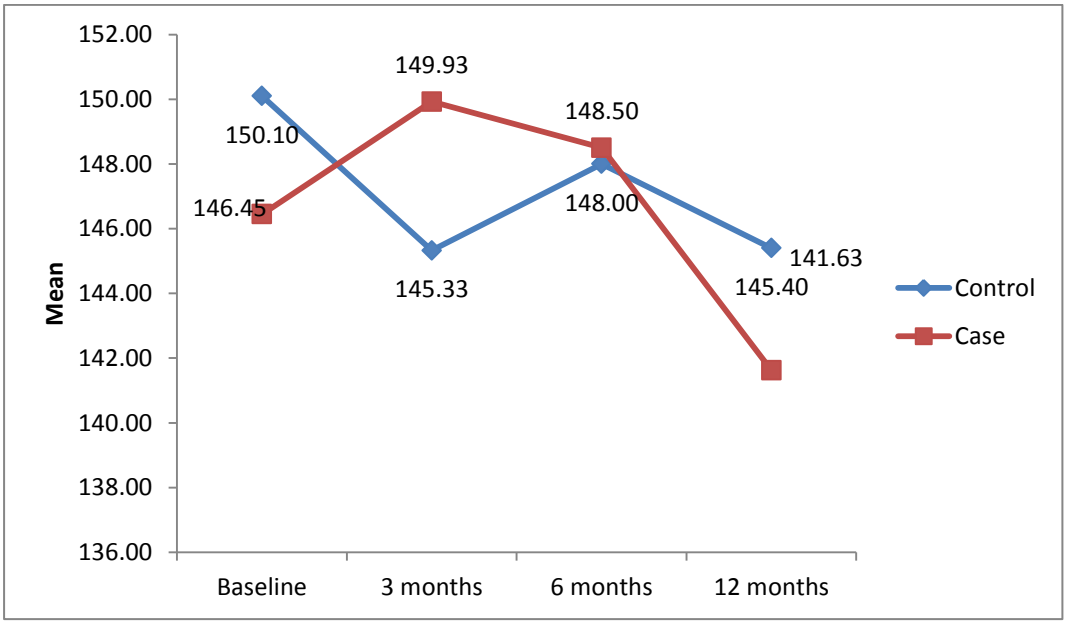


FIGURE 14: COMPARISON OF THE MEAN SERUM ALKALINE PHOSPHATASE VALUE

TABLE 15: COMPARISON OF THE MEAN PTH VALUES

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
iPTHpg/ml baseline	194.95	16.76	197.30	13.71	-0.686	0.495	-2.35	3.42
iPTH at 3 months	194.03	13.24	196.18	13.25	-0.726	0.470	-2.15	2.96
iPTH at 6 months	194.13	12.80	194.93	13.46	-0.272	0.786	-0.80	2.94
iPTH at 12 months	189.28	12.32	183.35	13.84	2.022	0.047	5.93	2.93

There was no difference in mean PTH level at baseline, 3 and 6 months between control and case group. PTH values were194.95, 194.03, 194.13, at baseline, 3, 6 and 12 months for controls. These were 197.30, 196.18, 194.93, at baseline, 3, and 6 months for cases. But there was statistically significance difference in mean PTH level between control and cases at 12 month (P=0.04)

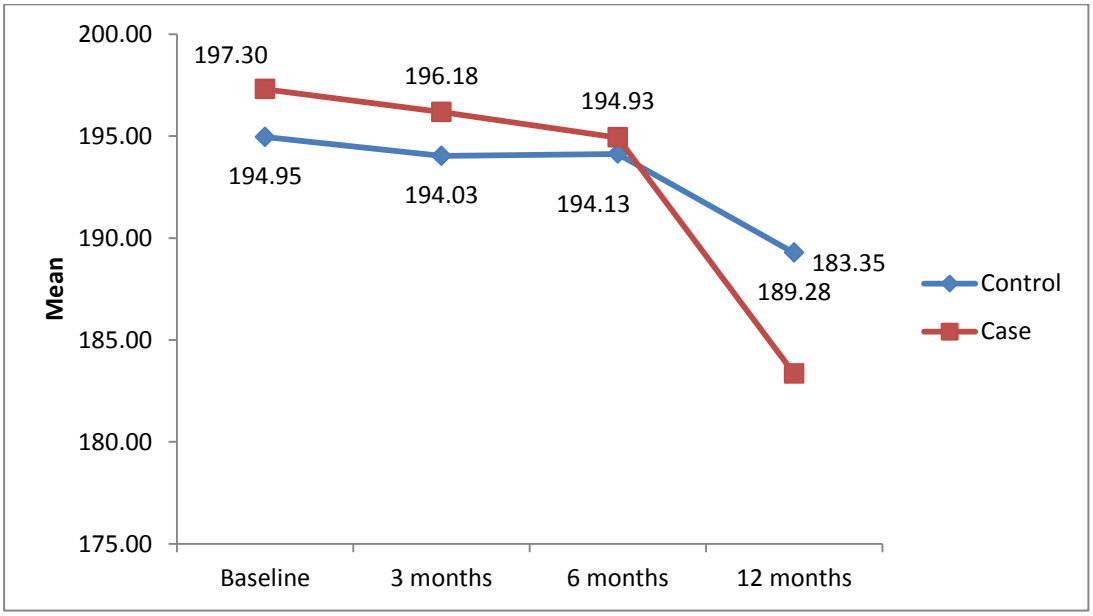


FIGURE 15: COMPARISON OF THE MEAN PTH VALUES

TABLE 16: COMPARISON OF DIFFERENCE IN MEAN PTH VALUE

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 3m	0.93	14.75	1.13	11.28	-0.068	0.946	-0.20	2.94
0- 6m	0.83	17.19	2.38	14.34	-0.438	0.663	-1.55	3.54
0-12m	5.68	18.60	13.95	16.86	-2.085	0.040	-8.28	3.97
3-6m	-0.10	12.96	1.25	11.45	-0.494	0.623	-1.35	2.73
3-12m	4.75	16.04	12.83	13.51	-2.435	0.017	-8.08	3.32
6-12m	4.85	12.34	11.58	10.80	-2.594	0.011	-6.73	2.59

There was statistically no difference in change in the mean value of PTH at 3, and 6 months between control and case group. But difference was significant at 12 months (P =0.04)

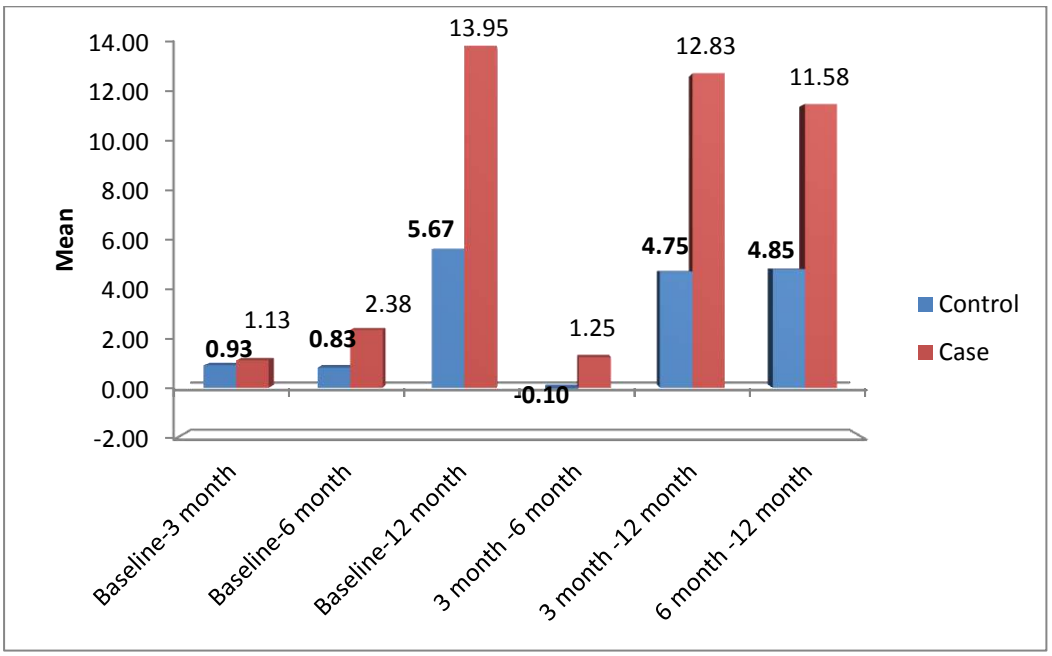


FIGURE 16: COMPARISON OF DIFFERENCE IN MEAN PTH VALUE

TABLE 17: COMPARISON OF THE MEAN VITAMIN D3 VALUES

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Vitamin D3 ng/ml baseline	25.18	3.66	25.25	3.22	-0.097	0.923	-0.07	0.77
Vitamin D3 at 3 months	26.15	3.15	25.70	2.54	0.703	0.484	0.45	0.64
Vitamin D3 at 6 months	25.80	3.33	26.18	2.83	-0.543	0.589	-0.38	0.69
Vitamin D3 at 12 months	25.90	2.78	24.53	3.62	1.904	0.061	1.38	0.72

There was no difference in mean vitamin D3 level at baseline, 3, 6 and 12 months between control and case group. This was 25.18, 26.15, 25.80, 25.90 at baseline, 3, 6 and 12 months for controls. This was 25.25, 25.70, 26.18, 24.53 at baseline, 3, 6 and 12 months for cases.

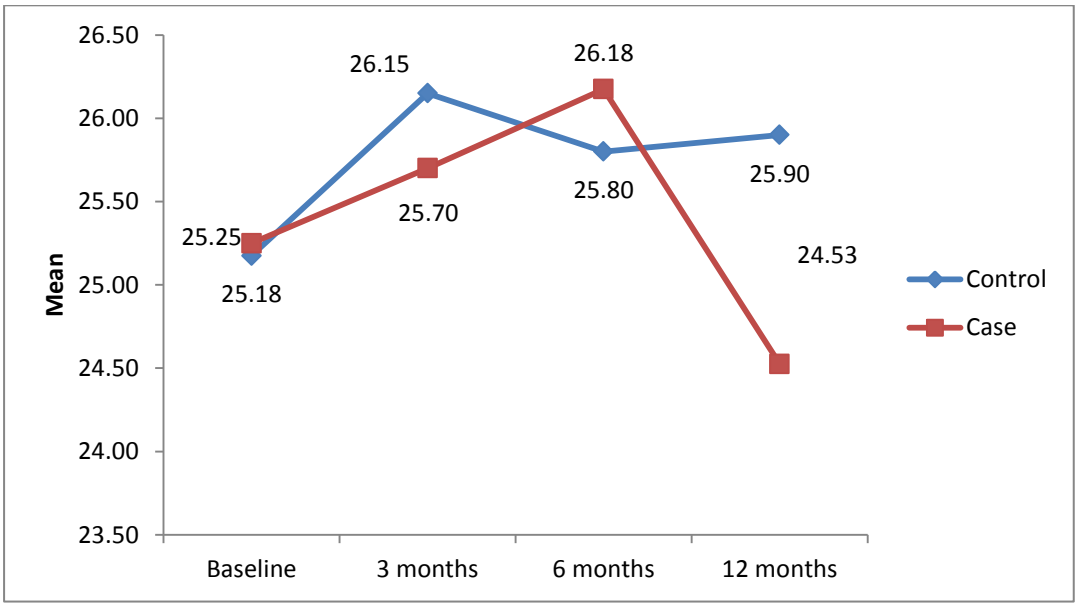


FIGURE 17: COMPARISON OF THE MEAN VITAMIN D3 VALUES

TABLE 18: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF LUMBAR SPINE

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
6 Month	0.12	0.17	-0.14	0.09	8.679	0.000	0.27	0.03
12 Month	0.25	0.24	-0.30	0.25	10.133	0.000	0.55	0.05

Mean lumbar spine T score was -1.42 for case and -1.41 for control respectively at baseline. It was -1.27 and -1.54 for case and control respectively at 6 months. It was-1.12 and -1.67for case and control respectively at 12 months.

There was improvement in mean T score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of T score was statistically significant between two groups at 6 and 12 month.

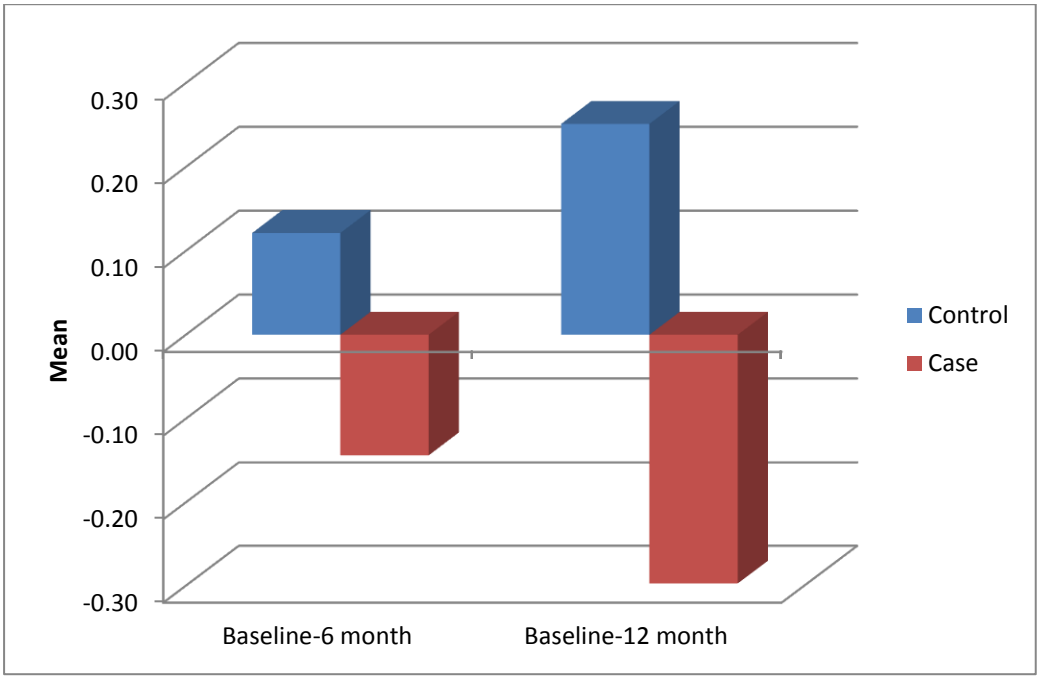


FIGURE 18: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF LUMBAR SPINE

TABLE 19: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF LUMBAR SPINE

	control		case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
6 Month	0.08	0.08	-0.13	0.06	13.112	0.000	0.20	0.02
12 Month	0.14	0.13	-0.29	0.28	8.863	0.000	0.43	0.05

Mean lumbar spine Z score was -0.61 for case and -0.43 for control respectively at baseline. It was -1.27 and -0.51 for case and control respectively at 6 months. It was -0.33 and -0.57for case and control respectively at 12 month.

There was improvement in mean Z score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

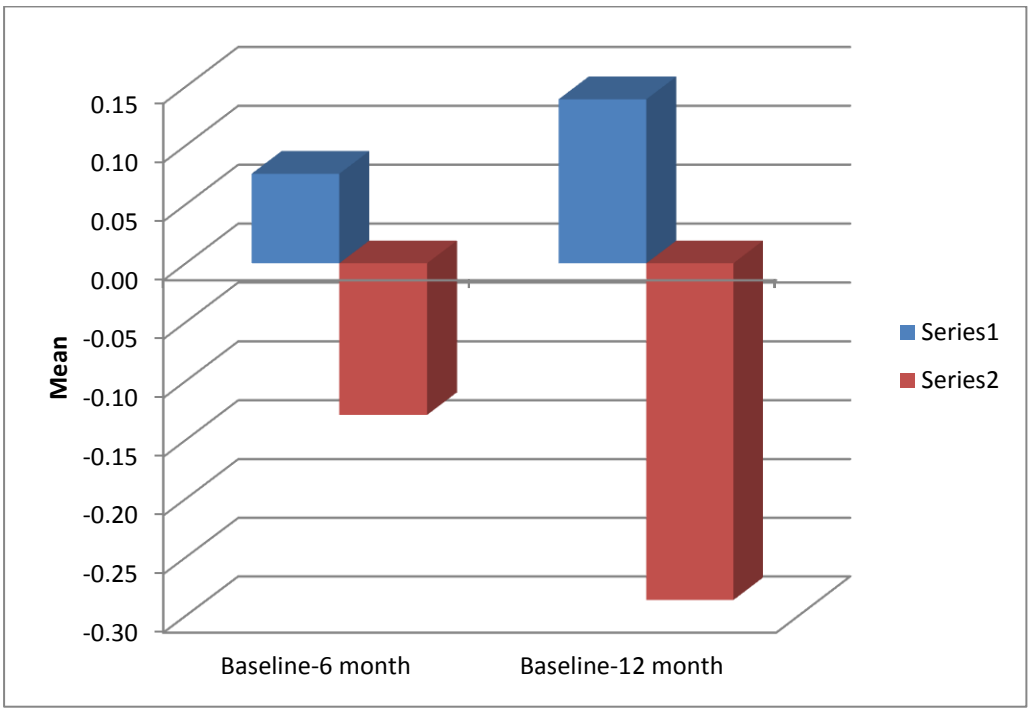


FIGURE 19: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF LUMBAR SPINE

TABLE 20: COMPARISON OF MEAN BMD AT LEVEL OF LUMBAR SPINE

	Control		Case		t	p-value	Difference	
	Mean g/cm2	SD	Mean	SD			Mean	SD
Baseline	1.13	0.26	1.05	0.18	1.651	0.103	0.08	0.05
6 month	1.09	0.26	1.14	0.20	-0.915	0.363	-0.05	0.05
12month	1.02	0.24	1.25	0.21	-4.692	0.000	-0.24	0.05
0- 6 Month	0.04	0.04	-0.09	0.08	9.833	0.000	0.13	0.01
0- 12 Month	0.12	0.09	-0.20	0.11	14.379	0.000	0.32	0.02

Mean lumbar spine Z BMD was 1.05 for case and 1.13 for control respectively at baseline. It was 1.14 and 1.09 for case and control respectively at 6 months. It was 1.25 and 1.02for case and control respectively at 12 month.

There was improvement in mean BMD at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in change in mean BMD was statistically significant between 2 groups at 6 and 12 month.

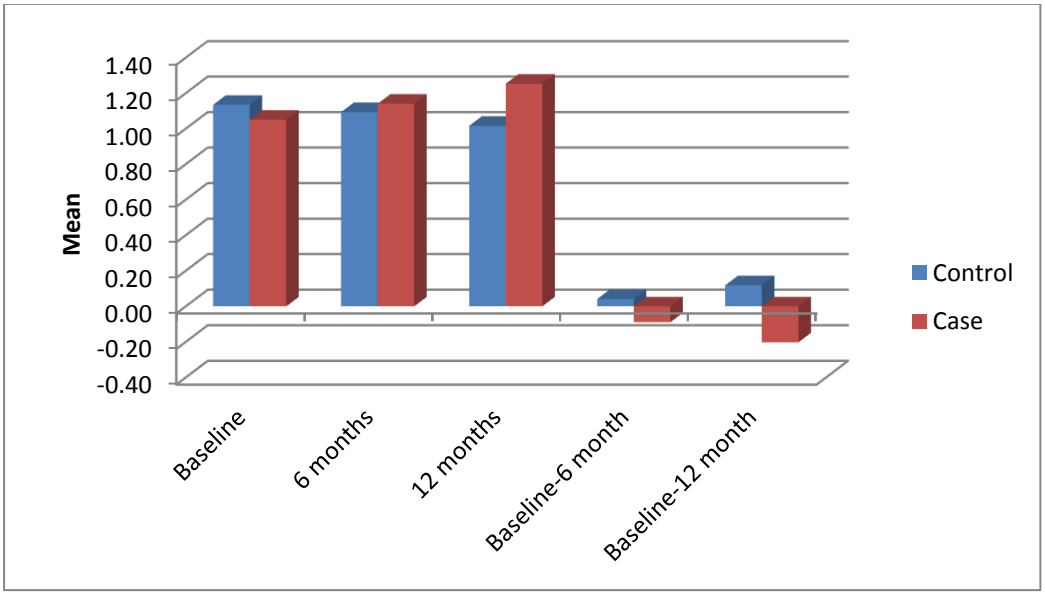


FIGURE 20: COMPARISON OF MEAN BMD AT LEVEL OF LUMBAR SPINE

TABLE 21: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF FEMUR NECK

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6 Month	0.08	0.15	-0.21	0.20	7.375	0.000	0.29	0.04
0- 12 Month	0.19	0.24	-0.40	0.20	11.880	0.000	0.59	0.05

Mean femur neck T score was -1.03 for case and -1.80 for control respectively at baseline. It was -1.82 and -1.88 for case and control respectively at 6 months. It was -1.63 and -1.99 for case and control respectively at 12 month.

There was improvement in mean T score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean T score was statistically significant between 2 groups at 6 and 12 month.

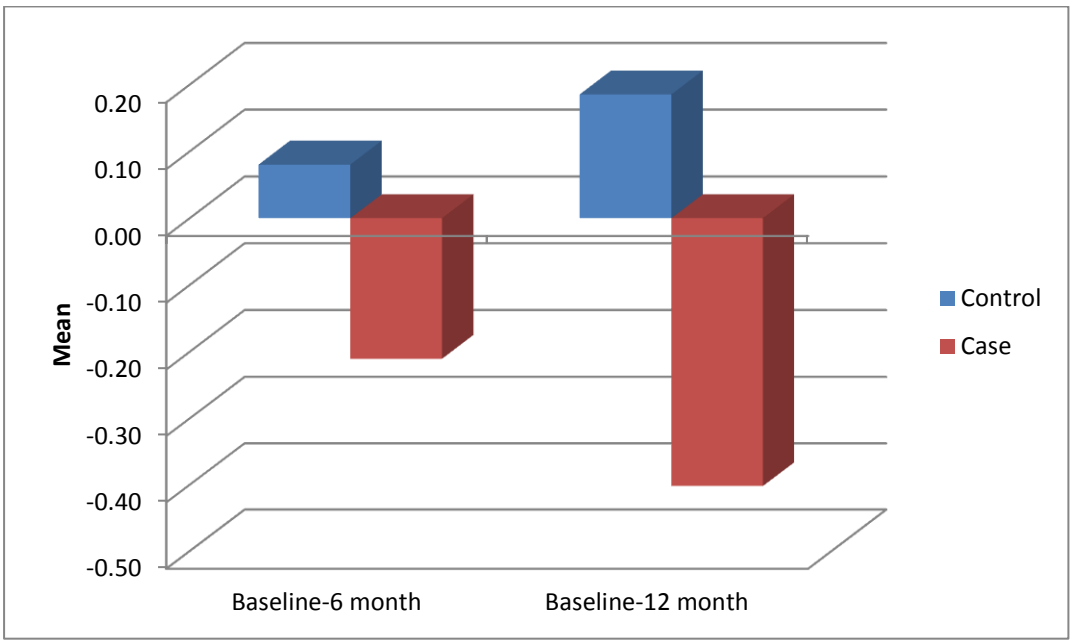


FIGURE 21: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF FEMUR NECK

TABLE 22: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF FEMUR NECK

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6 Month	0.06	0.09	-0.10	0.09	8.095	0.000	0.17	0.02
0-12 Month	0.17	0.15	-0.25	0.14	13.094	0.000	0.42	0.03

Mean femur neck Z score was -0.59 for case and -0.42 for control respectively at baseline. It was -0.49 and -0.48 for case and control respectively at 6 months. It was -0.34 and -0.59 for case and control respectively at 12 months.

There was improvement in mean Z score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean T score was statistically significant between 2 groups at 6 and 12 month.

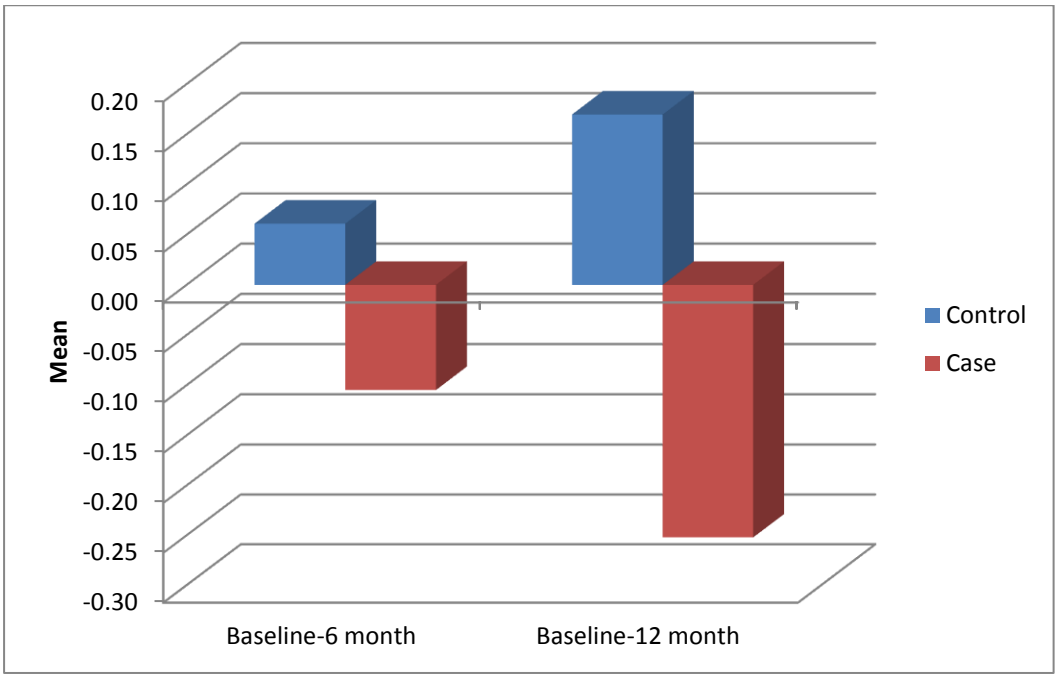


FIGURE 22: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF FEMUR NECK

TABLE 23: COMPARISON OF MEAN BMD AT LEVEL OF FEMUR NECK

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline	0.90	0.20	0.83	0.22	1.452	0.151	0.07	0.05
At 6 month	0.84	0.19	0.91	0.26	-1.336	0.185	-0.07	0.05
At 12 month	0.79	0.19	1.06	0.31	-4.632	0.000	-0.27	0.06
0- 6 Month	0.06	0.06	-0.08	0.09	8.323	0.000	0.14	0.02
0- 12 Month	0.11	0.09	-0.23	0.19	10.175	0.000	0.34	0.03

Mean femur neck BMD was 0.83 for case and 0.90 for control respectively at baseline. It was 0.91and 0.84 for case and control respectively at 6 months. It was 1.06 and 0.79for case and control respectively at 12 month.

There was improvement in mean BMD at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

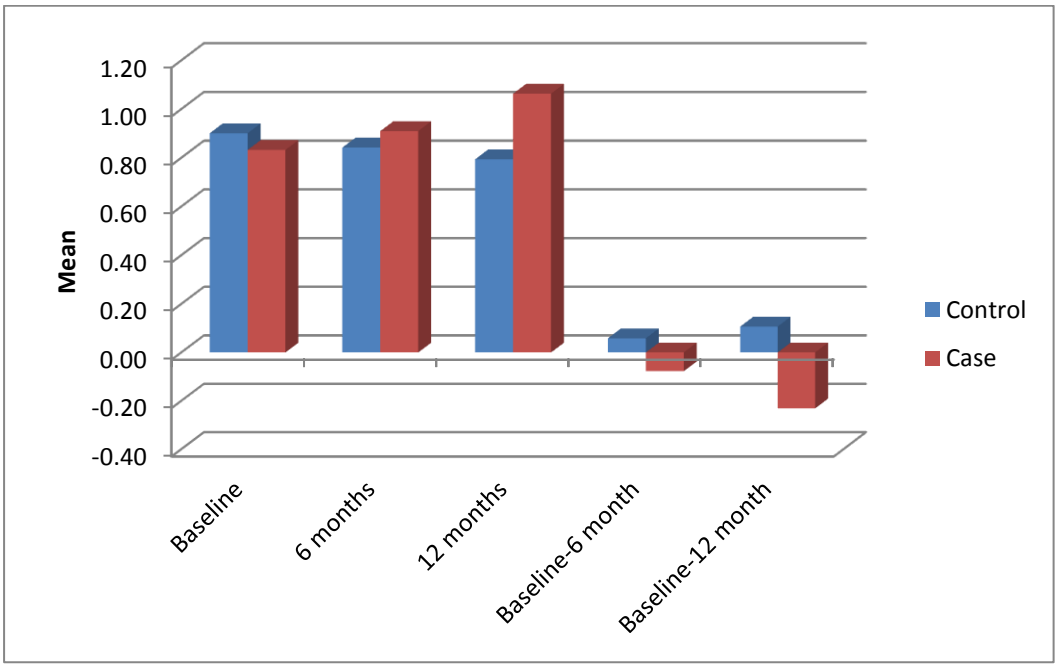


FIGURE 23: COMPARISON OF MEAN BMD AT LEVEL OF FEMUR NECK

TABLE 24: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE OF TOTAL HIP

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6 Month	0.09	0.11	-0.18	0.12	10.351	0.000	0.27	0.03
0- 12 Month	0.18	0.28	-0.35	0.16	10.541	0.000	0.53	0.05

Mean total hip T score was -1.78 for case and -1.49 for control respectively at baseline. It was -1.60 and -1.58 for case and control respectively at 6 months. It was -1.43 and -1.67for case and control respectively at 12 month.

There was improvement in mean T score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in the change in mean T score was statistically significant between 2 groups at 6 and 12 month.

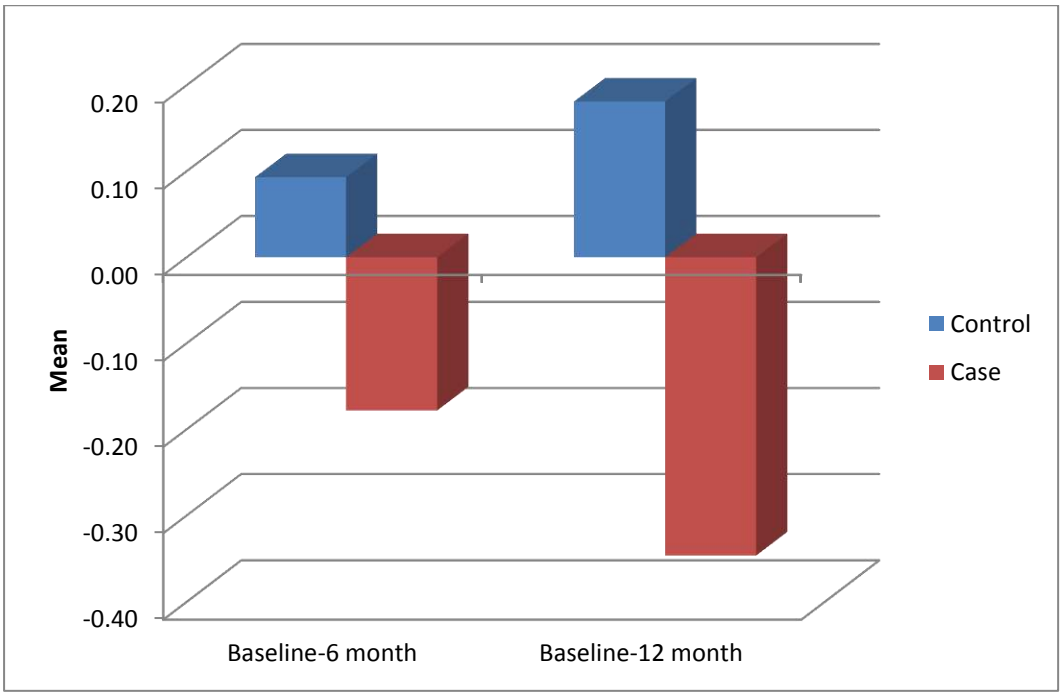


FIGURE 24: COMPARISON OFTHE DIFFERENCE OF MEAN T SCORE OF TOTAL HIP

TABLE 25: COMPARISON OFTHE DIFFERENCE OF MEAN Z SCORE OF TOTAL HIP

	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6 Month	0.06	0.11	-0.15	0.12	8.140	0.000	0.21	0.03
0- 12 Month	-0.10	0.83	-0.40	0.53	1.916	0.059	0.30	0.16

Mean total hip Z score was -0.93 for case and -0.57 for control respectively at baseline. It was -0.78 and -0.64 for case and control respectively at 6 months. It was -0.53 and -0.48 for case and control respectively at 12 months.

There was improvement in mean Z score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in change mean Z score was statistically significant between 2 groups at 6 month.

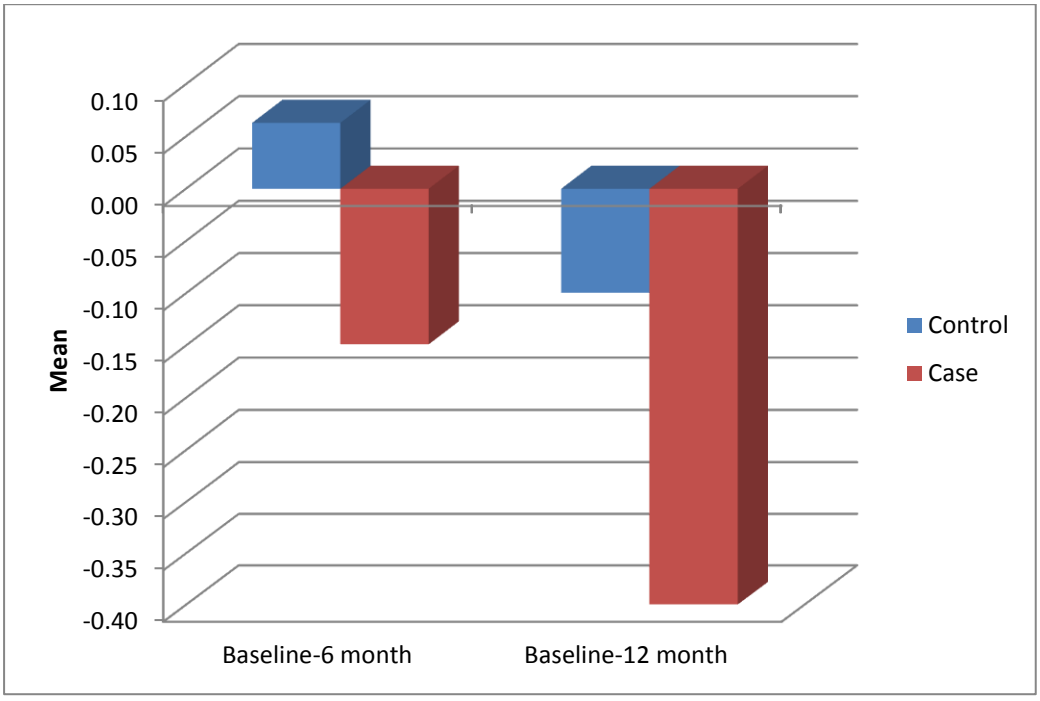


FIGURE 25: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE OF TOTAL HIP

TABLE 26: COMPARISON OF MEAN BMD OF TOTAL HIP

	Control		Case		t	p-value	Difference	
	Mean g/cm2	SD	Mean	SD			Mean	SD
Baseline	0.96	0.23	0.85	0.18	2.477	0.015	0.11	0.05
At 6 month	0.89	0.21	0.96	0.23	-1.452	0.151	-0.07	0.05
At 12 month	0.84	0.20	1.09	0.28	-4.615	0.000	-0.25	0.05
Difference 0- 6 Month	0.07	0.06	-0.12	0.10	9.899	0.000	0.19	0.02
Difference 0-12Month	0.12	0.10	-0.24	0.16	12.235	0.000	0.36	0.03

Mean total hip BMD was 0.85 for case and 0.96 for control respectively at baseline. It was 0.96and 0.89 for case and control respectively at 6 months. It was 1.09 and 0.84 for case and control respectively at 12 month.

There was improvement in mean BMD at level of total hip at 6 and 12 month in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in change in mean BMD was statistically significant between 2 groups at 6 and 12 month.

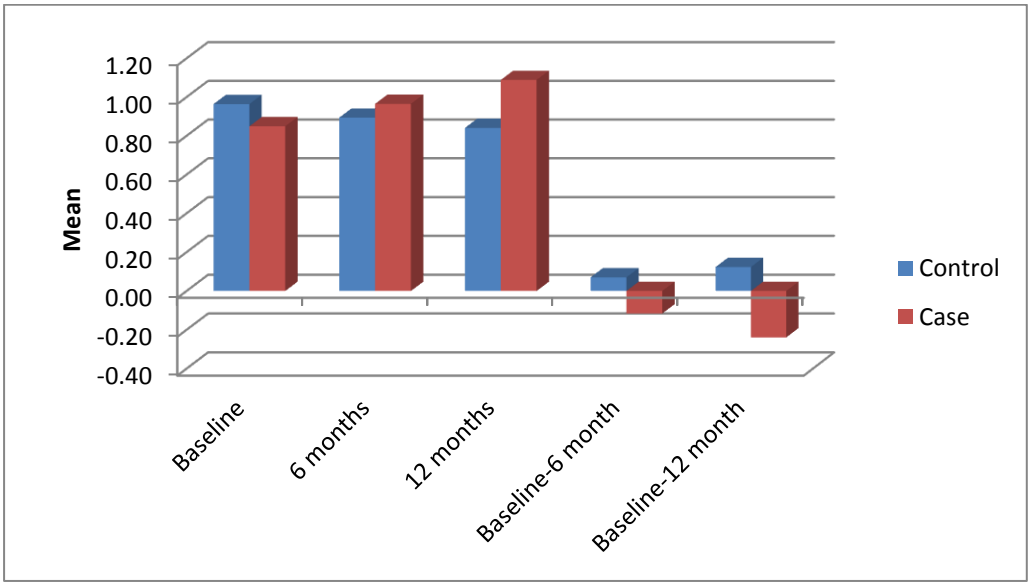
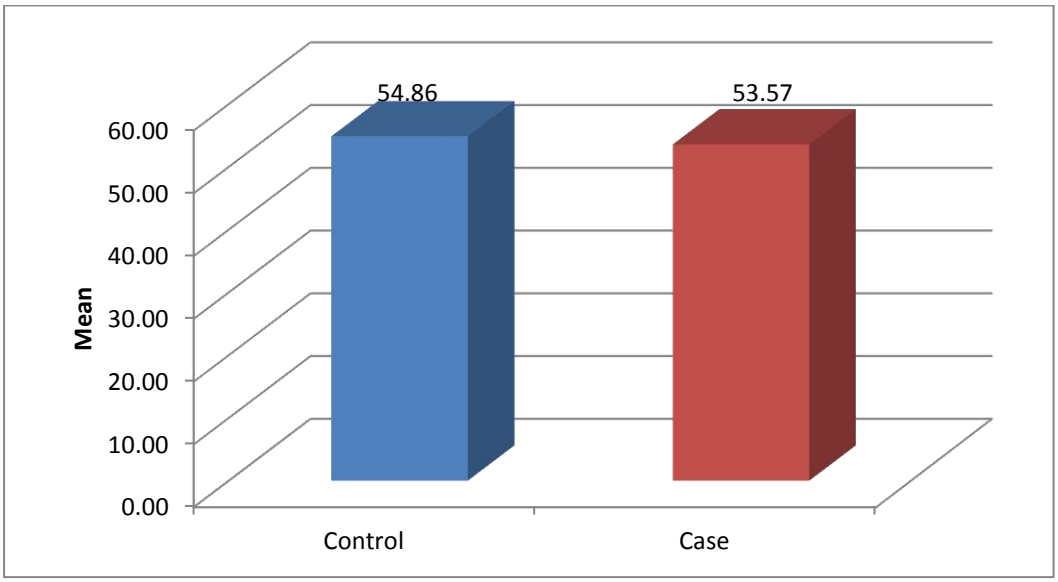


FIGURE 26: COMPARISON OF MEAN BMD OF TOTAL HIP

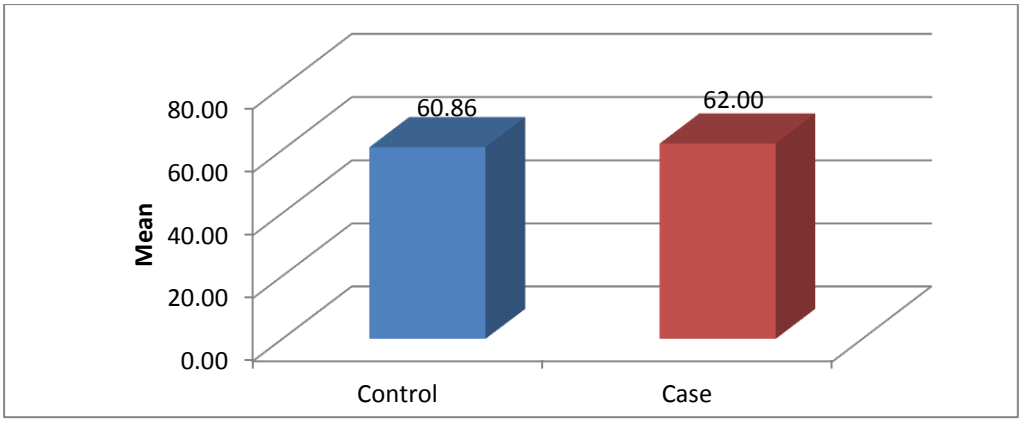
TABLE 27: COMPARISON OF BASELINE DEMOGRAPHIC FEATURES OF CKD 3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Age	54.86	13.13	53.57	12.39	0.188	0.854	1.29	6.83
Weight in Kg	60.86	5.05	62.00	5.45	-0.407	0.691	-1.14	2.81
Height in cm	166.43	4.04	167.29	1.11	-0.542	0.598	-0.86	1.58
SBP	128.86	5.01	123.43	7.55	1.585	0.139	5.43	3.42
DBP	81.14	6.20	80.86	6.52	0.084	0.934	0.29	3.40

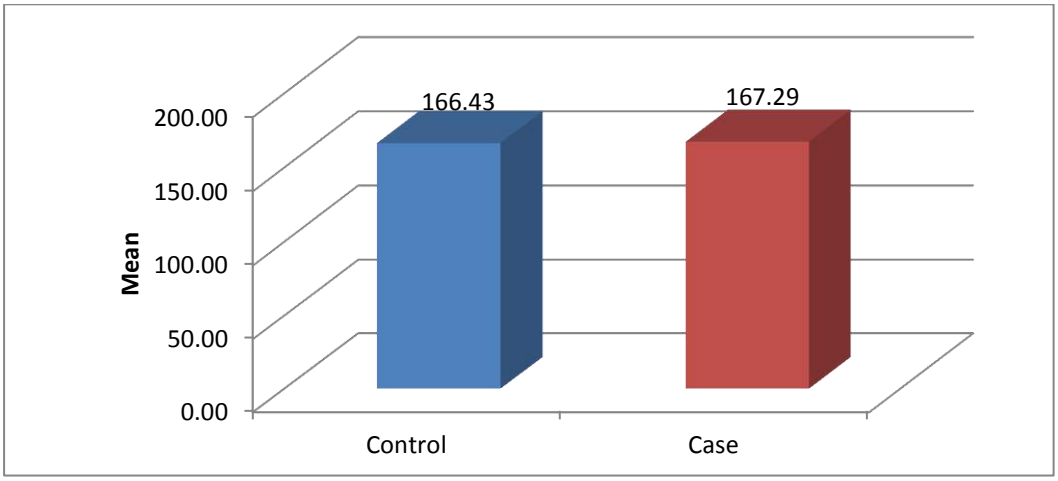
Mean age of control and case group was 54.86 (SD=13.13) and 53.57 (SD=12.39) respectively. There was statistically no difference between two groups in term of demographic features.



Mean weight of control and case group was 60.86(SD=5.04) and 62.00 (SD=5.45) respectively. There was statistically no difference between two groups.



Mean height of control and case group was 166.43(SD=4.04) and 167.29(SD=1.11) respectively. There was statistically no difference between two groups.



Mean SBP for control and case group was128.86 (SD= 5.01) and 123.43 (SD= 7.55) respectively. Mean DBP for control and case group was 81.14 (SD= 6.20) and 80.86 (SD= 6.52) respectively.

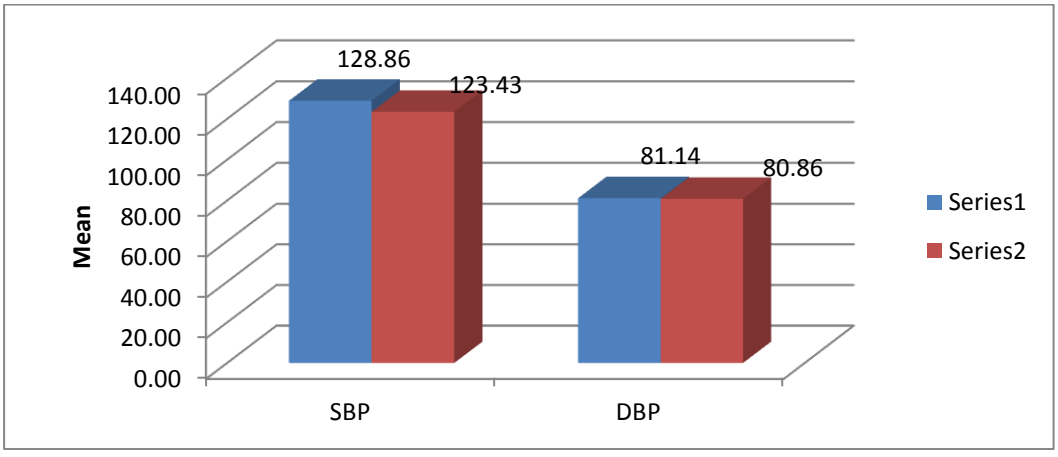


FIGURE 27: COMPARISON OF BASELINE DEMOGRAPHIC FEATURES OF CKD 3

TABLE 28: COMPARISON OF BASELINE COMPLETE BLOOD COUNTS OF CKD 3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Hemoglobin baseline g/dl	9.56	0.90	9.47	0.87	0.181	0.860	0.09	0.47
TLC baseline per ul	8.20	1.54	7.94	1.59	0.307	0.764	0.26	0.84
Platelets at baseline lakh	1.47	0.25	1.61	0.27	-0.993	0.340	-0.14	0.14

Baseline mean hemoglobin was 9.56 (SD= 0.90) and 9.47(SD= 0.87) for control and case group respectively. Baseline TLC was 8.2 (SD=1.54) and 7.94 (SD=1.59) for control and case group respectively. Baseline platelet count was 1.47 (SD=0.25) and 1.61 (SD=0.27) for control and case group respectively.

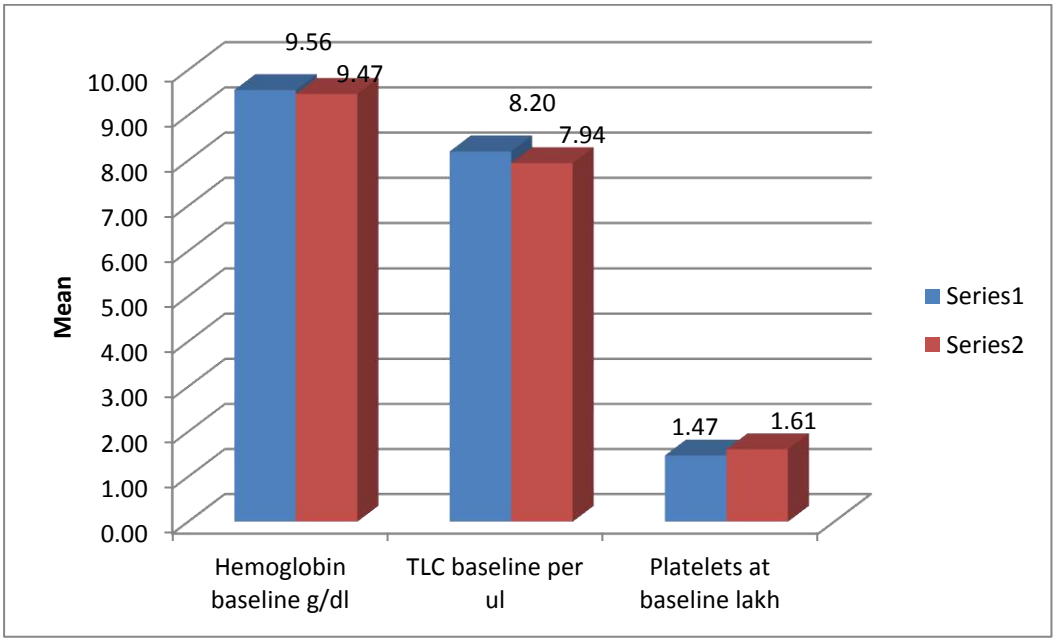
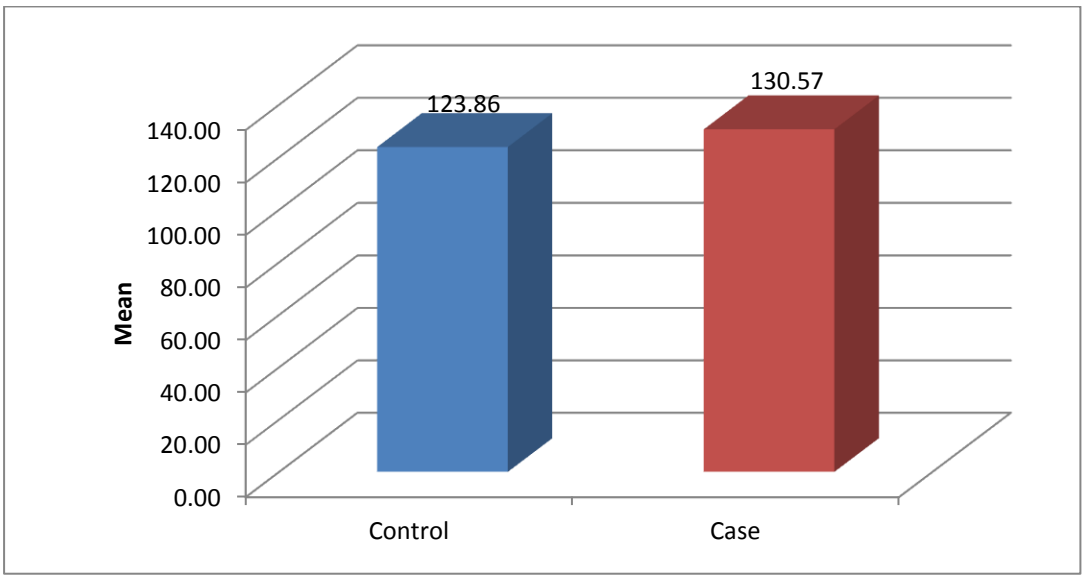


FIGURE 28: COMPARISON OF BASELINE COMPLETE BLOOD COUNTS OF CKD3

TABLE 29: COMPARISON OF THE MEAN UREA AND CREATININEAT BASELINEOF CKD 3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Urea at baseline mg/dl	123.86	18.29	130.57	18.60	-0.681	0.509	-6.71	9.86
Creatinine baseline mg/dl	2.29	0.63	1.99	0.41	0.944	0.364	0.60	0.64

Baseline mean urea was 123.86(SD= 18.29) and 130.57(SD= 18.60) for control and case group respectively. Baseline mean creatinine was 2.29 (SD= 0.63) and 1.99 (SD= 0.41) for control and case group respectively.



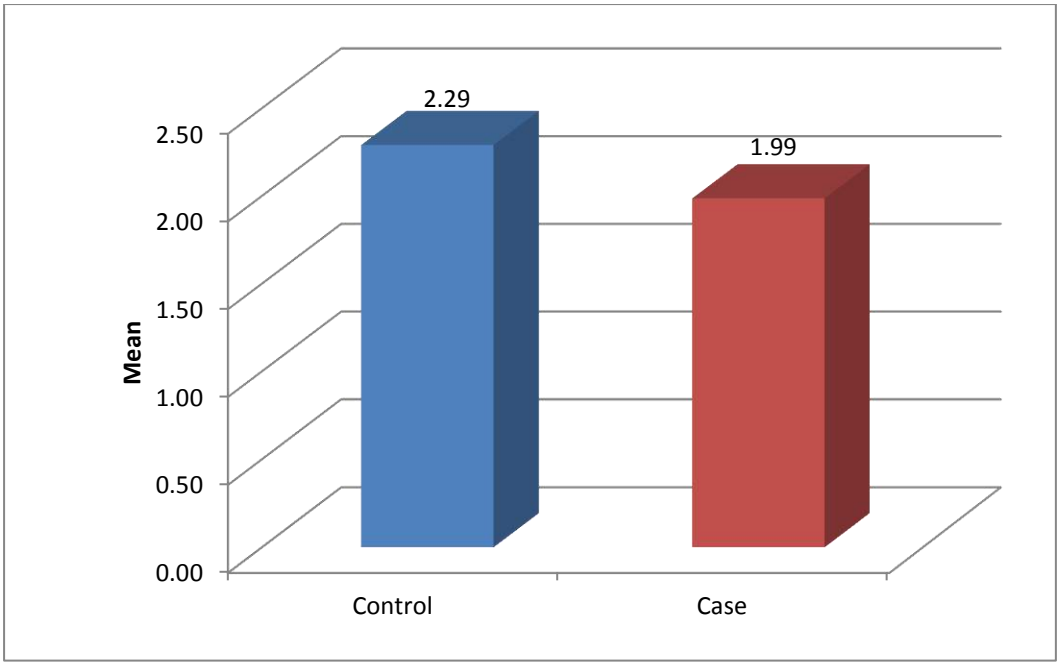
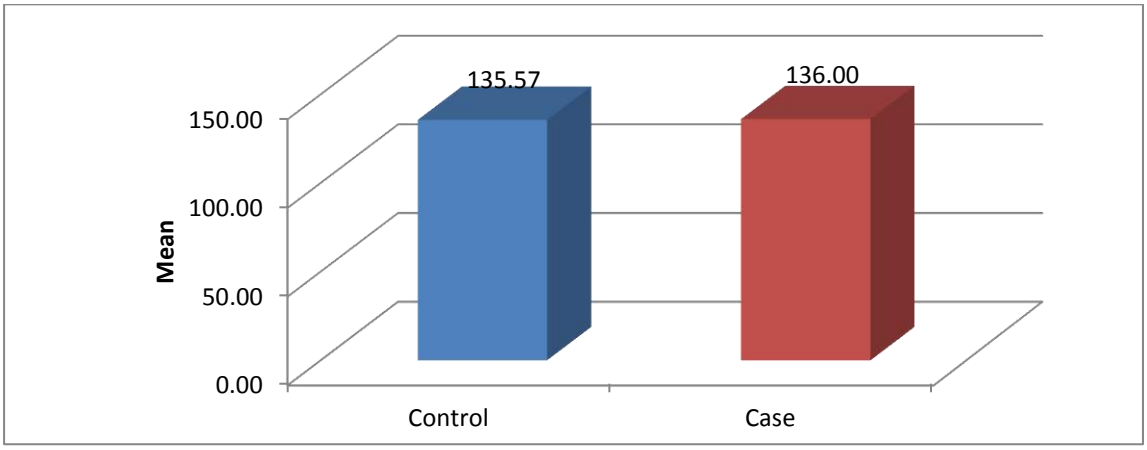


FIGURE 29: COMPARISON OF THE MEAN UREA AND CREATININEAT BASELINE OF CKD3

TABLE 30: COMPARISON OF THE MEAN SODIUM AND POTASSIUM AT BASELINEOF CKD3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Sodium baseline meq/l	135.57	6.13	136.00	6.53	-0.127	0.901	-0.43	3.39
Potassium at baseline meq/l	4.20	0.78	4.21	0.79	-0.034	0.973	-0.01	0.42

Baseline mean sodium was 135.57(SD= 6.13) and 136.00 (SD= 6.53) for control and case group respectively. Baseline mean potassium was 4.20 (SD= 0.78) and 4.21(SD= 0.79) for control and case group respectively.



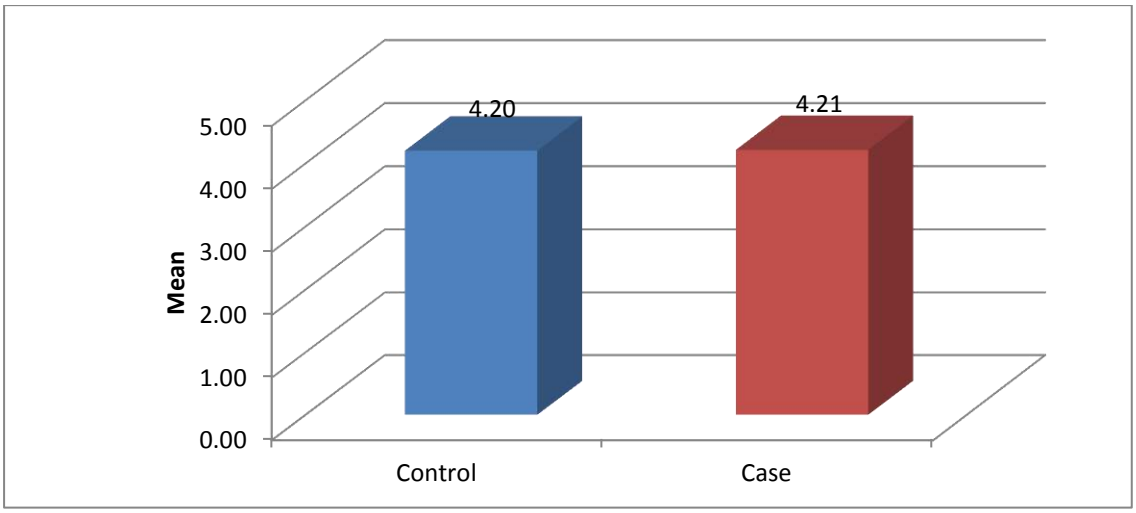


FIGURE 30: COMPARISON OF THE MEAN SODIUM AND POTASSIUM AT BASELINEOF CKD3

TABLE 31: COMPARISON OF THE MEAN CREATININE OF CKD 3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Creatinine baseline mg/dl	2.29	0.63	1.99	0.41	0.944	0.364	0.60	0.64
Creatinine at 3 months	2.31	0.76	2.03	0.35	0.905	0.383	0.29	0.32
creatinine at 6 months	2.59	1.03	2.16	0.34	1.043	0.317	0.43	0.41
creatinine at 12 months	2.94	1.42	2.31	0.38	1.131	0.280	0.63	0.56

Mean creatinine values were 2.29(SD=0.63), 2.31(SD=0.76), 2.59(SD=1.03) and 2.94 (1.42) at baseline, 3 months, 6months and 12 months respectively in control group. Mean creatinine values were 1.99(SD=0.41), 2.03(SD=0.35), 2.16(SD=0.34) and 2.31 (0.38) at baseline, 3 months, 6months and 12 months respectively in case group.

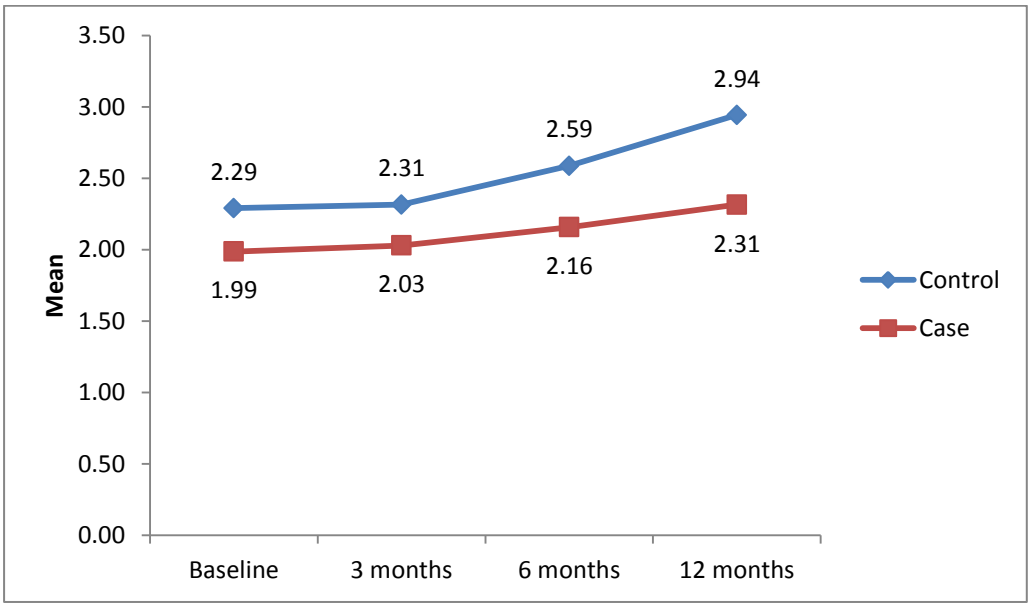


FIGURE 31: COMPARISON OF THE MEAN CREATININE OF CKD 3

TABLE 32a: COMPARISON OF THE DIFFERENCE OF MEAN CREATININE OF CKD3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 3m	0.27	0.94	-0.04	0.10	0.879	0.397	0.31	0.36
0- 6m	0.00	0.62	-0.17	0.14	0.715	0.488	0.17	0.24
0- 12m	-0.36	0.39	-0.33	0.16	-0.181	0.860	-0.03	0.16
3-6m	-0.27	0.34	-0.13	0.10	-1.085	0.299	-0.14	0.13
3-12m	-0.63	0.68	-0.29	0.11	-1.322	0.211	-0.34	0.26
6-12m	-0.36	0.43	-0.16	0.11	-1.196	0.255	-0.20	0.17

There was statistically no difference in change in the mean value of creatinine at 3, 6 and 12 months between control and case group. This was -0.27, -0.63, -0.36 at 3, 6 and 12 months for controls. This was -0.13, -0.29, -0.16at 3, 6 and 12 months for cases.

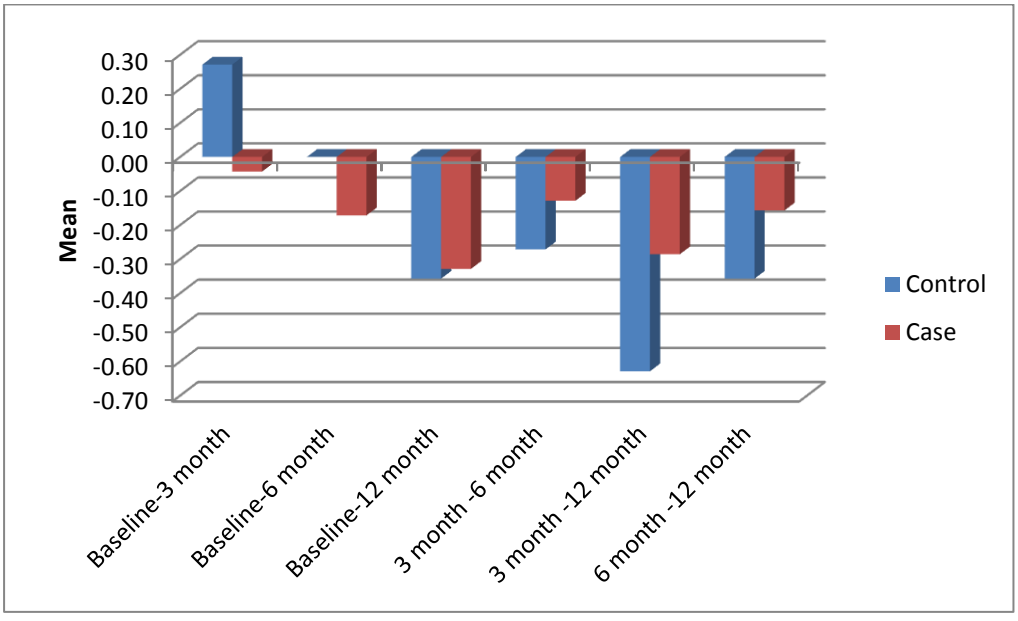


FIGURE 32a: COMPARISON OF THE DIFFERENCE OF MEAN CREATININE OF CKD3

TABLE 32b. PROGRESSION OF CKD3 TO CKD4

	Control	Case
Number	2	2
Percentage %	28.5	28.5

Total four patients, two each from case and control progressed from CKD3 to CKD4 stage at the end of one year.

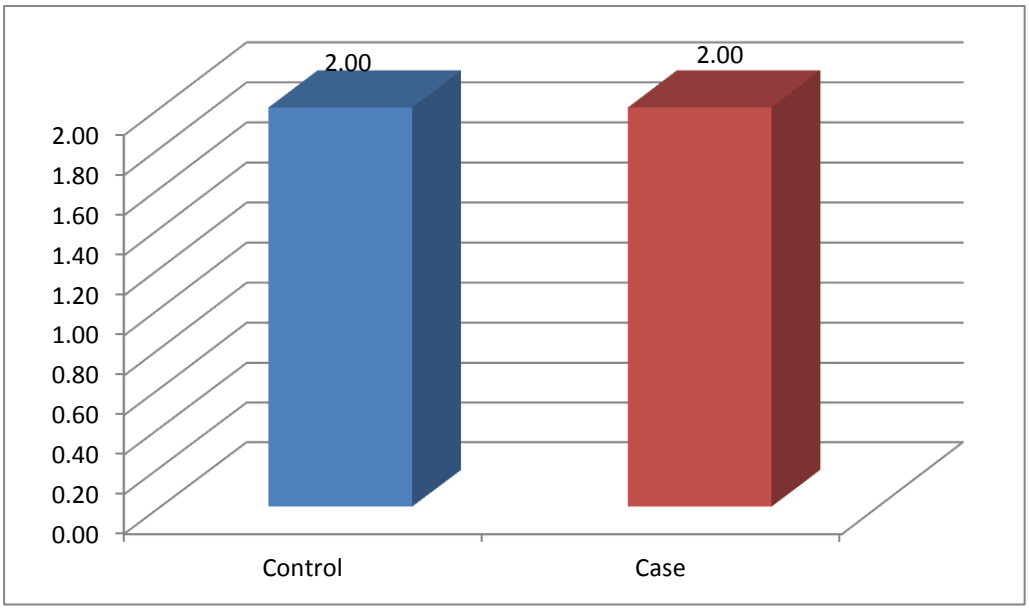


FIGURE 32b: PROGRESSION OF CKD3 TO CKD4

TABLE 32c. COMPARISON OF MEAN eGFR FOR CKD3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
eGFR baseline	35.86	7.56	38.14	5.18	-0.660	0.522	-2.29	3.46
eGFR at 12 months	29.71	7.63	31.57	3.60	-0.582	0.571	-1.86	3.19

There was no significant difference in mean e GFR between two groups at end of 12 months.

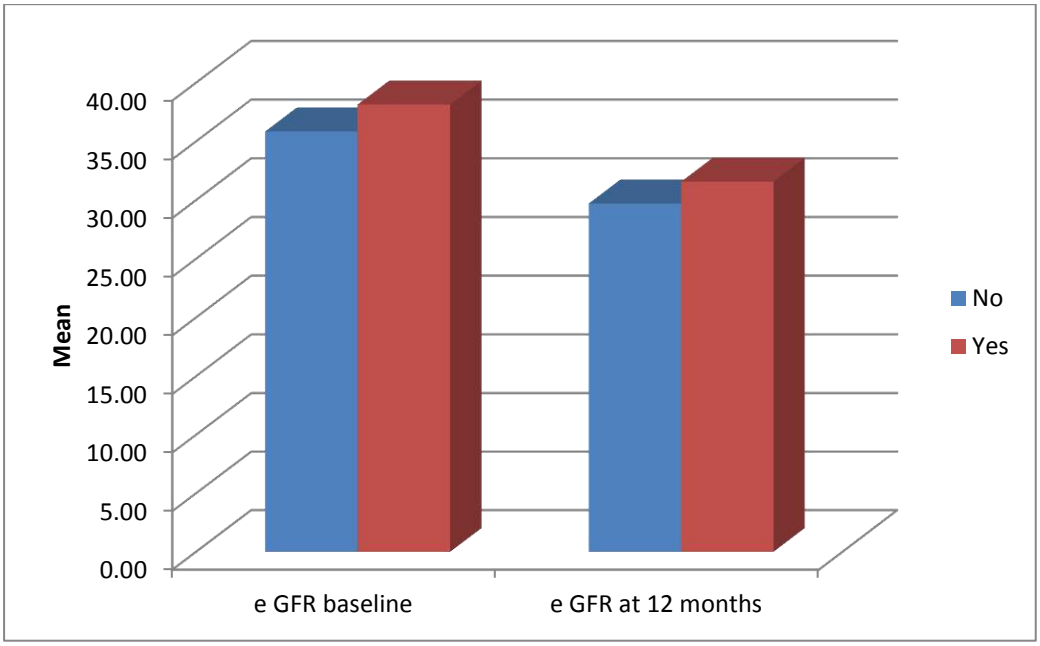


FIGURE 32c. COMPARISON OF MEAN e GFR FOR CKD3

TABLE 33: COMPARISON OF THE MEAN SERUM CALCIUM VALUE OF CKD 3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean mg/dl	SD	Mean	SD			Mean	SD
Calcium baseline	8.37	0.28	8.67	1.03	-0.743	0.472	-0.30	0.40
Calcium at 3 months	8.61	0.67	8.87	0.84	-0.634	0.538	-0.26	0.41
Calcium at 6 months	8.80	0.69	8.36	0.96	0.990	0.342	0.44	0.45
Calcium at 12 months	9.17	0.80	8.57	1.06	1.197	0.254	0.60	0.50

There was no difference in mean calcium level at baseline, 3, 6 and 12 months between control and case group. This was 8.37, 8.61, 8.80, 9.17 at baseline, 3, 6 and 12 months for controls. This was 8.67, 8.87, 8.36, 8.57 at baseline, 3, 6 and 12 months for cases.

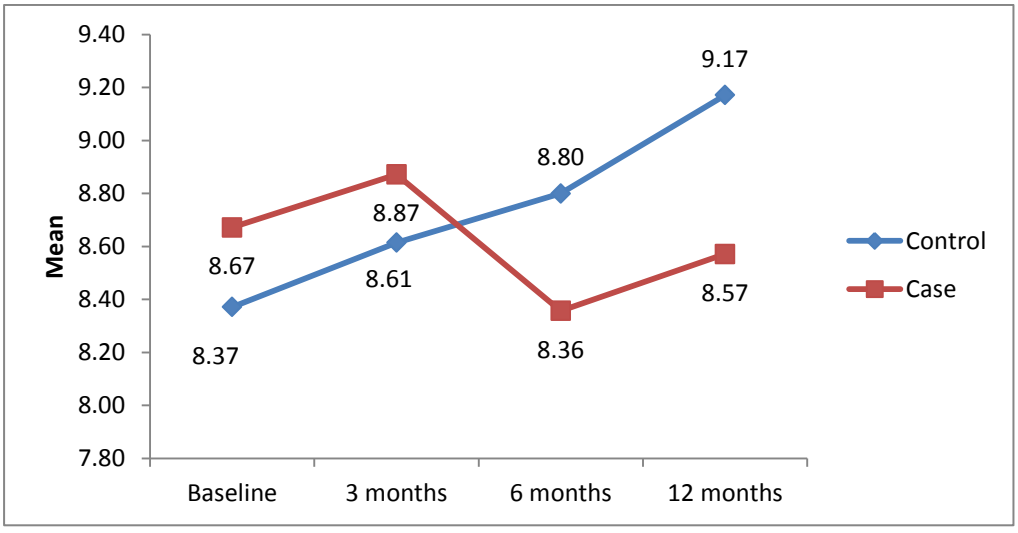


FIGURE 33: COMPARISON OF THE MEAN SERUM CALCIUM VALUE OF CKD 3

TABLE 34: COMPARISON OF THE MEAN SERUM PHOSPHORUS VALUE OF CKD3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean mg/dl	SD	Mean	SD			Mean	SD
Phosphorus baseline	6.41	0.83	6.60	0.77	-0.435	0.672	-0.19	0.43
Phosphorus at 3 months	6.20	0.35	6.79	0.69	-2.004	0.068	-0.59	0.29
Phosphorus at 6 months	6.56	0.82	7.34	1.76	-1.070	0.306	-0.79	0.73
Phosphorus at 12 months	6.56	0.87	6.43	1.54	0.193	0.850	0.13	0.67

There was no difference in mean phosphorus level at baseline, 3, 6 and 12 months between control and case group. This was 6.41, 6.20, 6.56, 6.56 at baseline, 3, 6 and 12 months for controls. This was 6.60, 6.79, 7.34, 6.43 at baseline, 3, 6 and 12 months for cases.

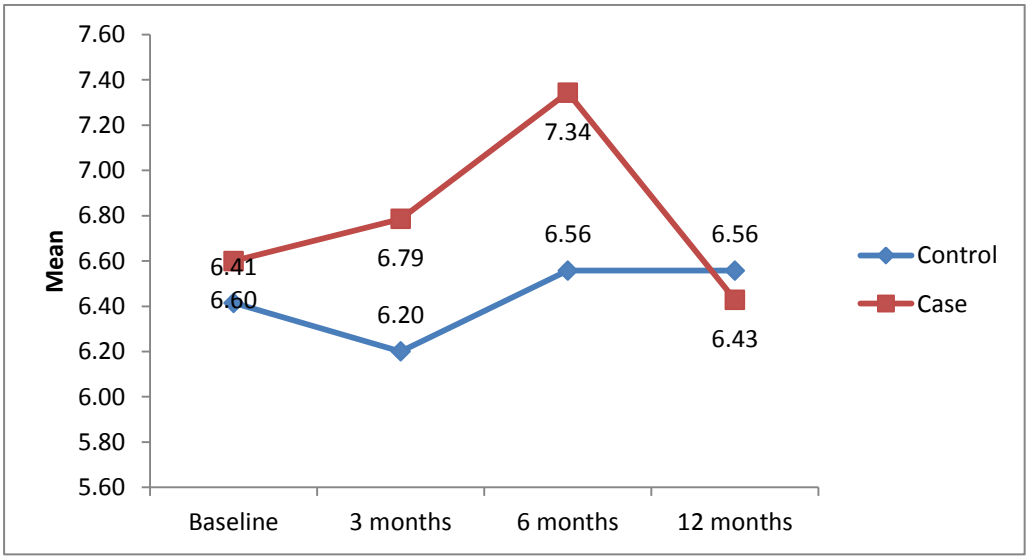


FIGURE 34: COMPARISON OF THE MEAN SERUM PHOSPHORUS VALUE OF CKD 3

TABLE 35: COMPARISON OF THE MEAN SERUM ALKALINE PHOSPHATASE VALUE OF CKD3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean U/dl	SD	Mean	SD			Mean	SD
Base line	144.14	12.02	148.57	8.87	-0.784	0.448	-4.43	5.65
At 3 month	144.57	9.02	145.57	12.90	-0.168	0.869	-1.00	5.95
At 6 month	148.71	11.66	156.57	10.18	-1.343	0.204	-7.86	5.85
At 12 month	141.71	8.48	151.29	10.67	-1.858	0.088	-9.57	5.15

There was no difference in mean ALP level at baseline, 3, 6 and 12 months between control and case group. This was 144.14, 144.57, 148.71, 141.71 at baseline, 3, 6 and 12 months for controls. This was 148.57, 145.57,156. 57, 151.29 at baseline, 3, 6 and 12 months for cases.

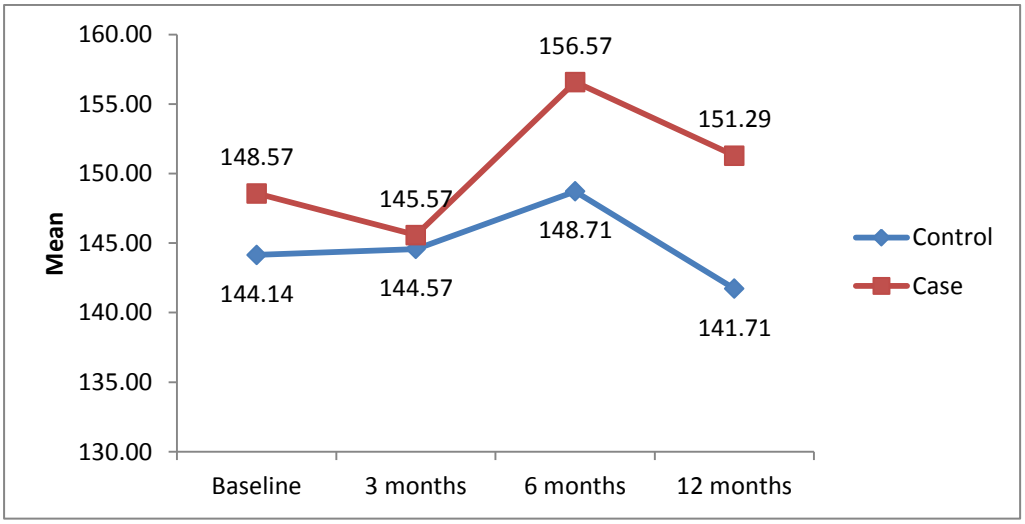


FIGURE 35: COMPARISON OF THE MEAN SERUM ALKALINE PHOSPHATASE VALUE OF CKD3

TABLE 36: COMPARISON OF THE MEAN VITAMIN D3 VALUES OF CKD 3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean mg/ml	SD	Mean	SD			Mean	SD
Baseline	25.57	2.15	25.00	2.77	0.431	0.674	0.57	1.32
At 3 month	25.86	2.67	25.14	2.85	0.483	0.638	0.71	1.48
At 6 month	26.29	2.56	26.86	2.48	-0.424	0.679	-0.57	1.35
At 12 month	25.71	2.87	25.14	2.85	0.374	0.715	0.57	1.53

There was no difference in mean vitamin D3 level at baseline, 3, 6 and 12 months between control and case group. This was 25.57, 25.86, 26.29, 25.71 at baseline, 3, 6 and 12 months for controls. This was 25.00, 25.14, 26.86, 25.14 at baseline, 3, 6 and 12 months for cases.

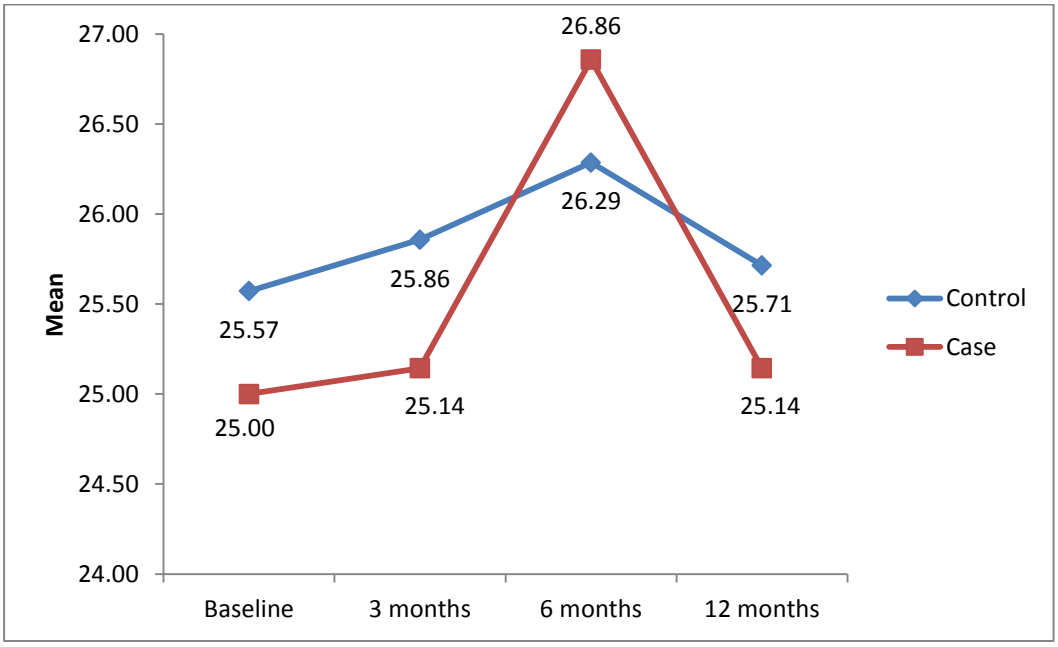


FIGURE 36: COMPARISON OF THE MEAN VITAMIN D3 VALUES OF CKD 3

TABLE 37: COMPARISON OF THE MEAN PTH VALUES OF CKD 3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean pg/ml	SD	Mean	SD			Mean	SD
IPTH baseline	193.00	13.44	199.71	9.91	-1.064	0.308	-6.71	6.31
iPTH at 3 months	190.00	9.95	198.71	12.07	-1.474	0.166	-8.71	5.91
iPTH at 6 months	194.14	11.54	194.86	14.36	-0.103	0.920	-0.71	6.96
iPTH at 12 months	186.43	8.94	182.29	11.00	0.773	0.454	4.14	5.36

There was statistically no difference in mean PTH level at baseline, 3, 6 and 12 months between control and case group of CKD3. PTH values were193.00, 190.00, 194.14, 186.43, at baseline, 3, 6 and 12 months for controls. These were199.71, 198.71, 194.86, 182.29 at baseline, 3, 6 and 12months for cases.

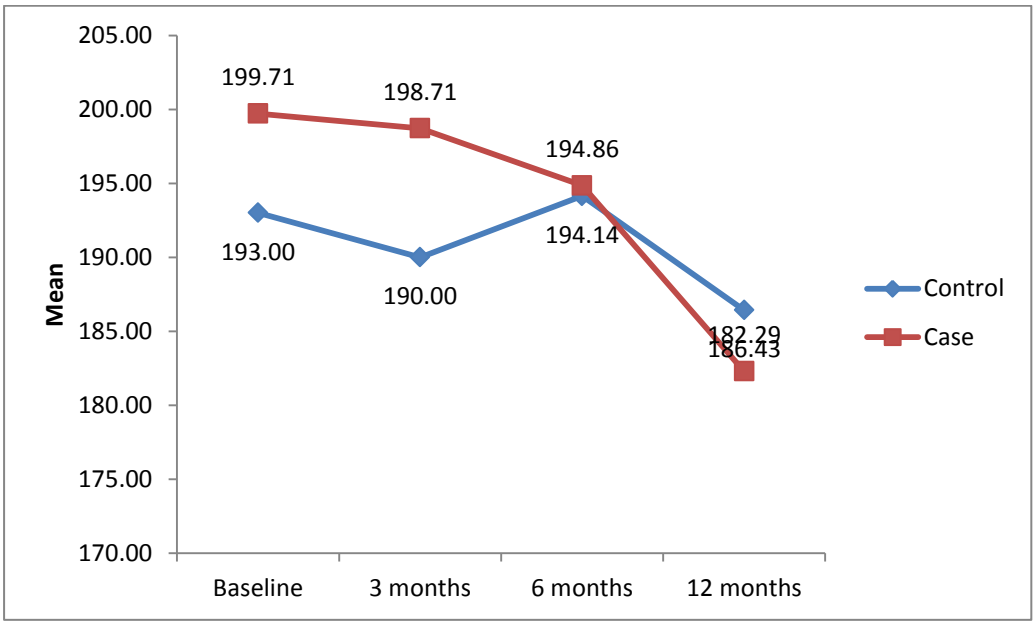


FIGURE 37: COMPARISON OF THE MEAN PTH VALUES OF CKD 3

TABLE 38: COMPARISON OF DIFFERENCE IN MEAN PTH VALUE OF CKD 3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-3m	3.00	8.76	1.00	4.08	0.548	0.594	2.00	3.65
0- 6m	-1.14	10.57	4.86	14.47	-0.886	0.393	-6.00	6.77
0-12m	6.57	16.84	17.43	11.54	-1.407	0.185	-10.86	7.72
3-6m	-4.14	11.20	3.86	17.32	-1.026	0.325	-8.00	7.79
3-12m	3.57	15.34	16.43	14.48	-1.613	0.133	-12.86	7.97
6-12m	7.71	10.42	12.57	8.30	-0.964	0.354	-4.86	5.04

There was statistically no difference in change in the mean value of PTH at 3, 6 and 12 months between control and case group.

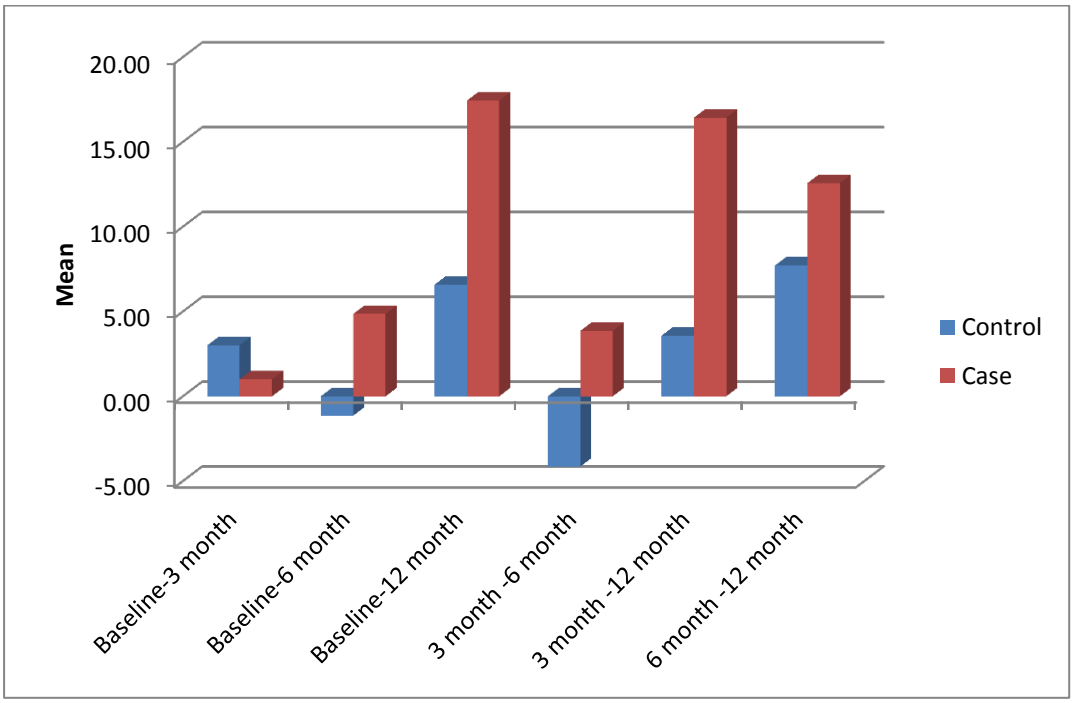


FIGURE 38: COMPARISON OF DIFFERENCE IN MEAN PTH VALUE OF CKD 3

TABLE 39: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF LUMBAR SPINE OF CKD3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6M	0.10	0.06	-0.14	0.05	8.167	0.000	0.24	0.03
0-12M	0.23	0.08	-0.19	0.44	2.454	0.030	0.42	0.17

Mean lumbar spine T score was -0.03 for case and -1.11 for control respectively at baseline. It was -0.79 and -1.21 for case and control respectively at 6 months. It was -0.74 and -1.34 or case and control respectively at 12 months. There was improvement in mean T score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of T score was statistically significant between 2 groups at 6 and 12 month.

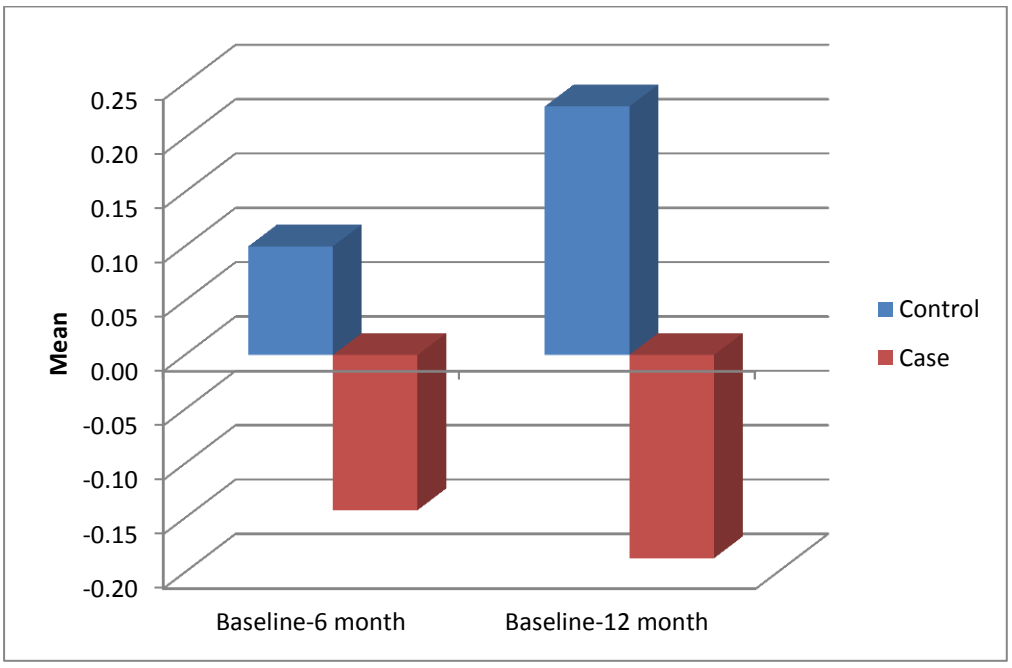


FIGURE 39: COMPARISON OF MEAN T SCORE AT LEVEL OF LUMBAR SPINE OF CKD3

TABLE 40: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF LUMBAR SPINE OF CKD3

CKD3 stage	control		case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6 Month	0.07	0.05	-0.14	0.08	6.124	0.000	0.21	0.03
0-12 Month	0.17	0.13	-0.23	0.14	5.731	0.000	0.40	0.07

Mean lumbar spine Z score was -0.24 for case and -0.23 for control respectively at baseline. It was -0.10 and -0.30 for case and control respectively at 6 months. It was -0.01 and -0.40for case and control respectively at 12 months.

There was improvement in mean Z score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of Z score was statistically significant between 2 groups at 6 and 12 month.

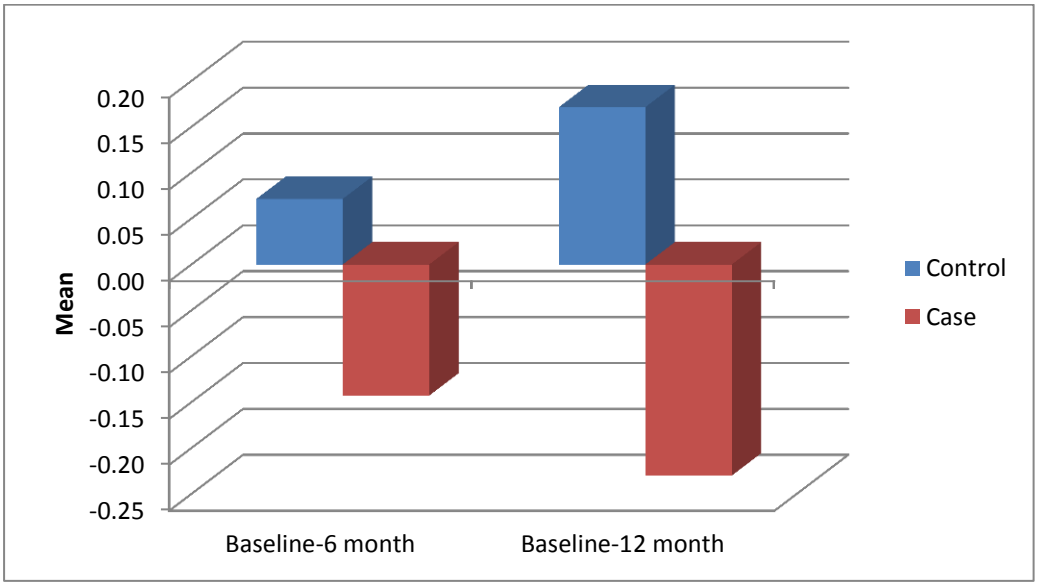


FIGURE 40: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF LUMBAR SPINE

TABLE 41: COMPARISON OF MEAN BMD AT LEVEL OF LUMBAR SPINE OF CKD3

CKD 3 stage	control		case		t	p-value	Difference	
	Mean g/cm2	SD	Mean	SD			Mean	SD
Baseline	1.11	0.12	1.02	0.18	1.160	0.268	0.09	0.08
At 6 Month	1.08	0.11	1.17	0.21	-1.028	0.324	-0.09	0.09
At 12Month	1.00	0.13	1.30	0.18	-3.657	0.003	-0.30	0.08
DIFFERENCE 0- 6 M	0.03	0.01	-0.15	0.06	7.699	0.000	0.19	0.02
DIFFERENCE 0-12 M	0.12	0.06	-0.28	0.07	11.269	0.000	0.40	0.04

Mean lumbar spine BMD was 1.02 for case and 1.11 for control respectively at baseline. It was 1.17 and 1.08 for case and control respectively at 6 months. It was 1.30 and 1.01for case and control respectively at 12 month.

There was improvement in mean BMD at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in the change in mean was statistically significant between 2 groups at 6 and 12 month.

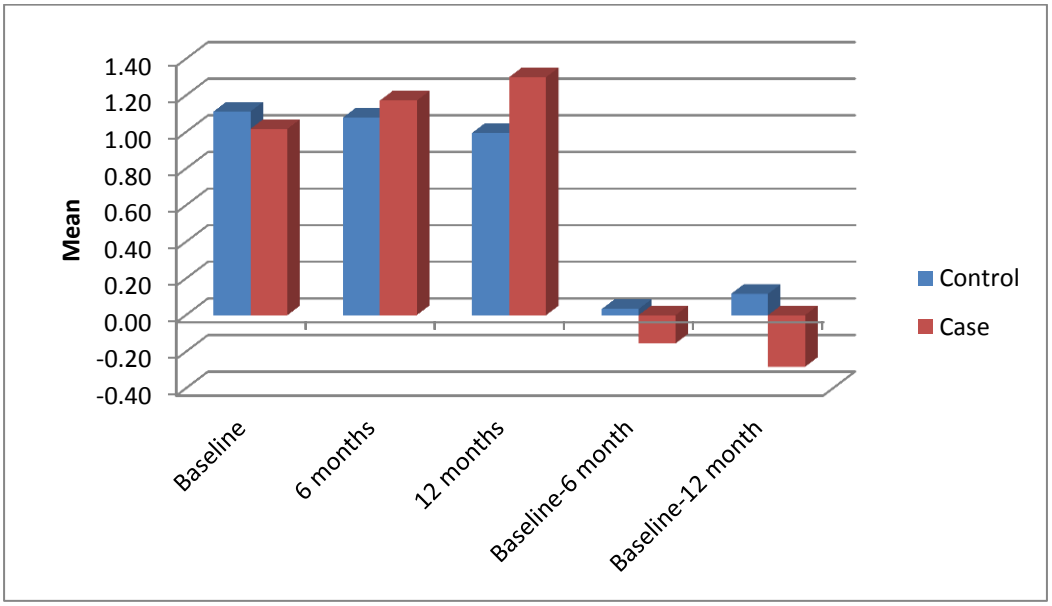


FIGURE 41: COMPARISON OF MEAN BMD AT LEVEL OF LUMBAR SPINE OF CKD 3

TABLE 42: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF FEMUR NECK OF CKD3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6M	0.07	0.05	-0.20	0.08	7.550	0.000	0.27	0.04
0-12M	0.19	0.07	-0.44	0.10	13.914	0.000	0.63	0.05

Mean femur neck T score was -1.66 for case and -1.41 for control respectively at baseline. It was -1.46 and -1.49 for case and control respectively at 6 months. It was -1.21 and -1.60 for case and control respectively at 12 month.

There was improvement in mean T score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean T score was statistically significant between 2 groups at 6 and 12 month.

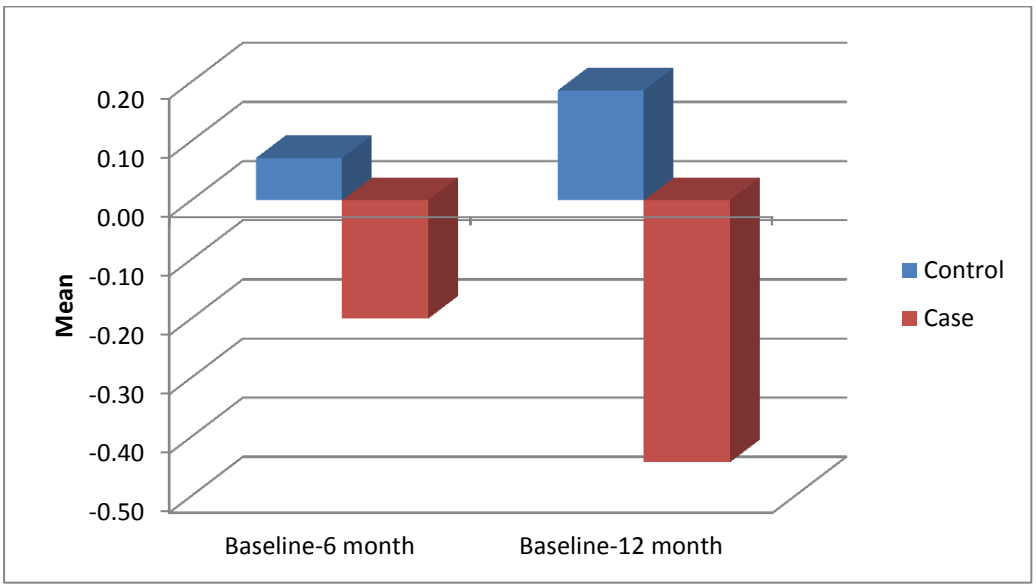


FIGURE 42: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF FEMUR NECK OF CKD 3

TABLE 43: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF FEMUR NECK OF CKD3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6M	0.06	0.08	-0.09	0.07	3.612	0.004	0.14	0.04
0-12M	0.19	0.17	-0.24	0.13	5.388	0.000	0.43	0.08

Mean femur neck Z score was -0.21 for case and -0.21 for control respectively at baseline. It was -0.13 and -0.27 for case and control respectively at 6 months. It was -0.03 and -0.40 for case and control respectively at 12 months.

There was improvement in mean Z score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean T score was statistically significant between 2 groups at 6 and 12 month.

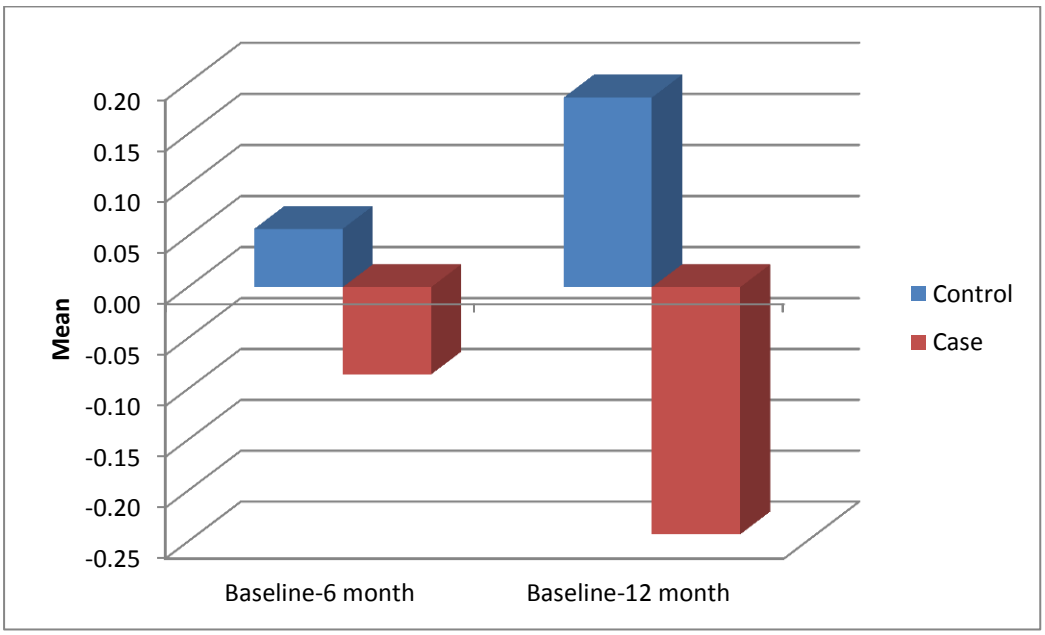


FIGURE 43: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF FEMUR NECK OF CKD 3

TABLE 44: COMPARISON OF MEAN BMD AT LEVEL OF FEMUR NECK OF CKD3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean g/cm2	SD	Mean	SD			Mean	SD
Baseline	1.10	0.18	0.93	0.14	2.029	0.065	0.18	0.09
At 6 month	1.01	0.18	1.00	0.20	0.083	0.936	0.01	0.10
At 12 month	0.95	0.18	1.37	0.32	-3.000	0.011	-0.42	0.14
DIFFERENCE 0-6 Month	0.09	0.06	-0.07	0.07	4.628	0.001	0.17	0.04
DIFFERENCE 0-12 Month	0.15	0.10	-0.44	0.32	4.701	0.001	0.59	0.13

Mean femur neck BMD was 0.93 for case and 1.10 for control respectively at baseline. It was 1.00 and 1.01 for case and control respectively at 6 months. It was 1.37 and 0.95for case and control respectively at 12 month.

There was improvement in mean BMD at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in the change in mean BMD was statistically significant between 2 groups at 6 and 12 month.

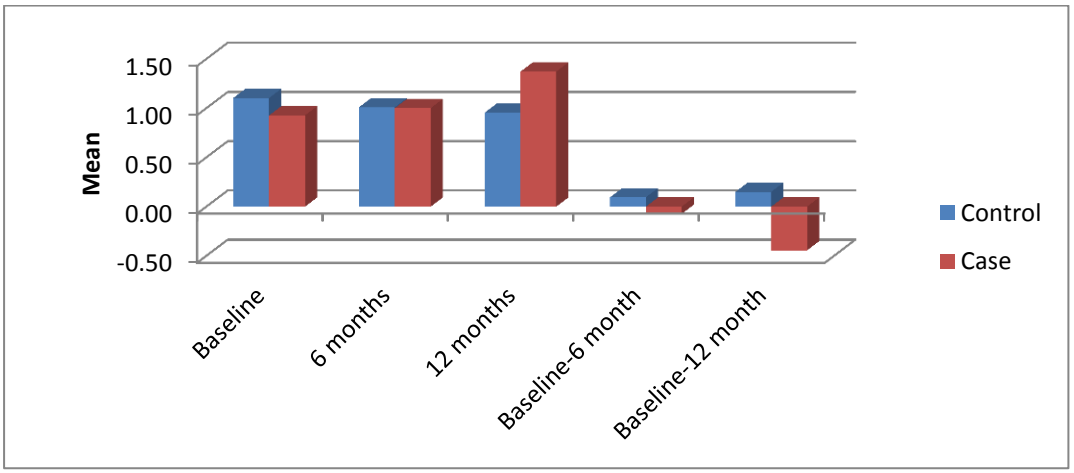


FIGURE 44: COMPARISON OF MEAN BMD AT LEVEL OF FEMUR NECK OF CKD3

TABLE 45: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE OF TOTAL HIP OF CKD 3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6 Month	0.09	0.15	-0.17	0.09	3.955	0.002	0.26	0.07
0-12 Month	0.13	0.28	-0.33	0.10	4.133	0.001	0.46	0.11

Mean total hip T score was -1.39 for case and -1.21 for control respectively at baseline. It was -1.21 and -1.30 for case and control respectively at 6 months. It was -1.06 and -1.34for case and control respectively at 12 month.

There was improvement in mean T score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in the change in mean T score was statistically significant between 2 groups at 6 and 12 month.

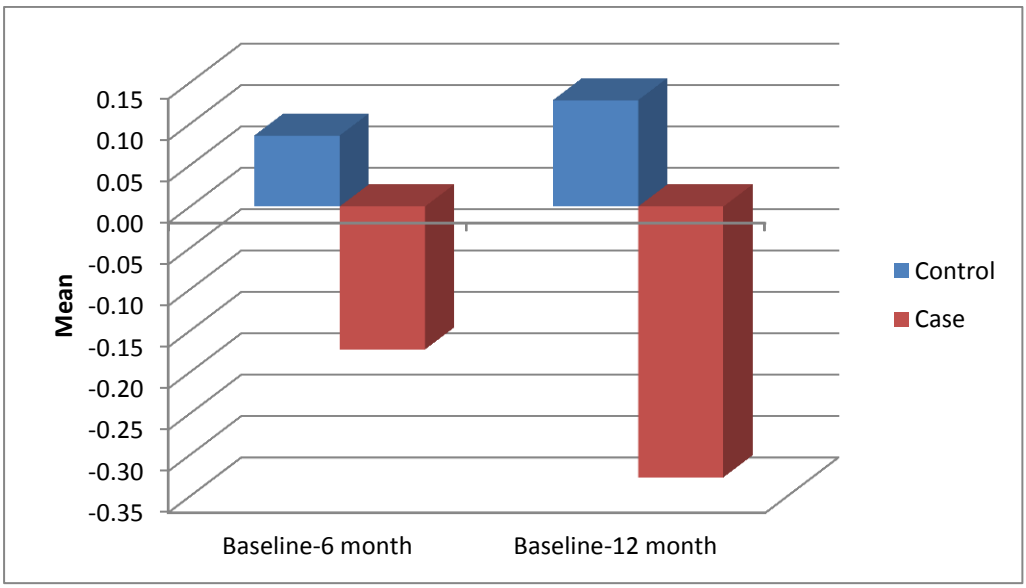


FIGURE 45: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE OF TOTAL HIP OF CKD3

TABLE 46: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE OF TOTAL HIPOF CKD 3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6 Month	0.07	0.13	-0.13	0.05	3.934	0.002	0.20	0.05
0-12 Month	0.17	0.22	-0.31	0.15	4.843	0.000	0.49	0.10

Mean total hip Z score was -0.34 for case and -0.43 for control respectively at baseline. It was -0.21 and -0.50 for case and control respectively at 6 months. It was -0.03 and -0.60 for case and control respectively at 12 months.

There was improvement in mean Z score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in the change in mean Z score was statistically significant between 2 groups at 6 and 12 month.

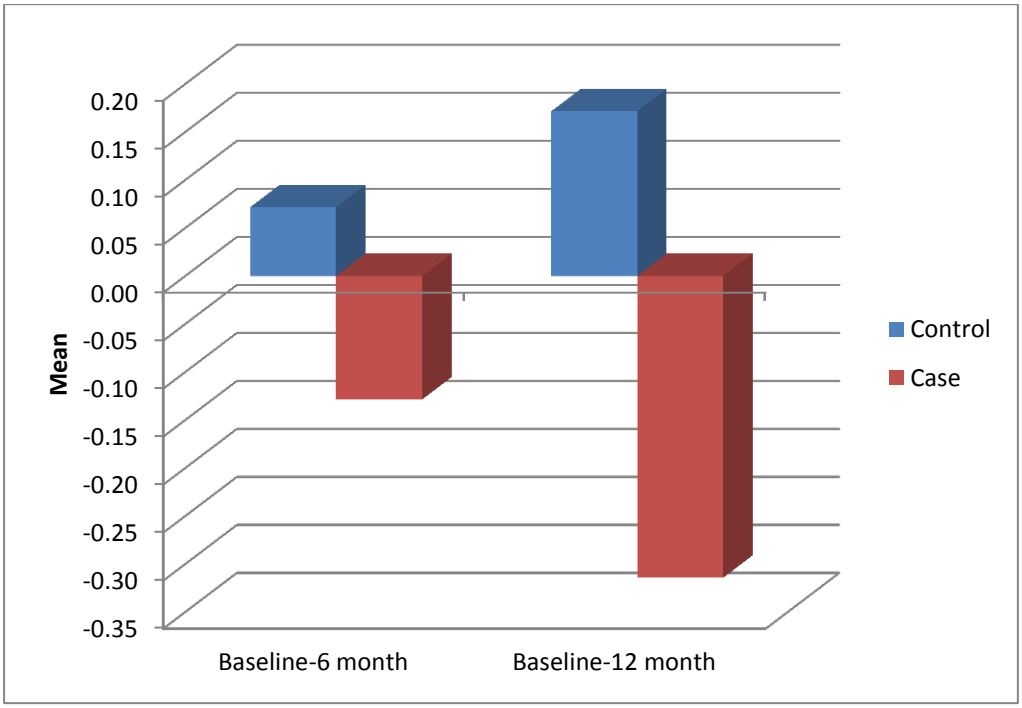


FIGURE 46: COMPARISON OFTHE DIFFERENCE OF MEAN Z SCORE OF TOTAL HIP OF CKD

TABLE 47: COMPARISON OF MEAN BMD OF TOTAL HIP OF CKD3

CKD 3 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline	1.13	0.19	1.00	0.22	1.116	0.286	0.12	0.11
At 6 month	1.05	0.15	1.18	0.22	-1.321	0.211	-0.13	0.10
At 12 month	0.98	0.12	1.32	0.25	-3.289	0.006	-0.34	0.10
DIFFERENCE 0- 6 Month	0.08	0.05	-0.18	0.12	5.218	0.000	0.25	0.05
DIFFERENCE 0- 12 Month	0.15	0.09	-0.31	0.16	6.610	0.000	0.46	0.07

Mean total hip BMD was 0.22 for case and 1.13 for control respectively at baseline. It was 1.18 and 1.05 for case and control respectively at 6 months. It was 1.32 and 0.98 for case and control respectively at 12 month.

There was improvement in mean BMD at level of total hip at 6 and 12 month in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in change in mean BMD was statistically significant between 2 groups at 6 and 12 month.

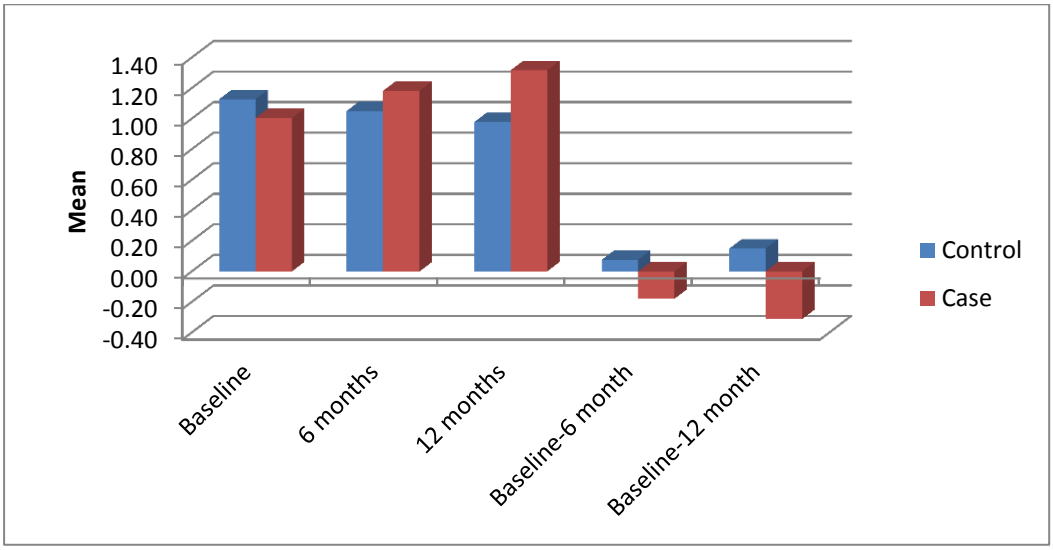
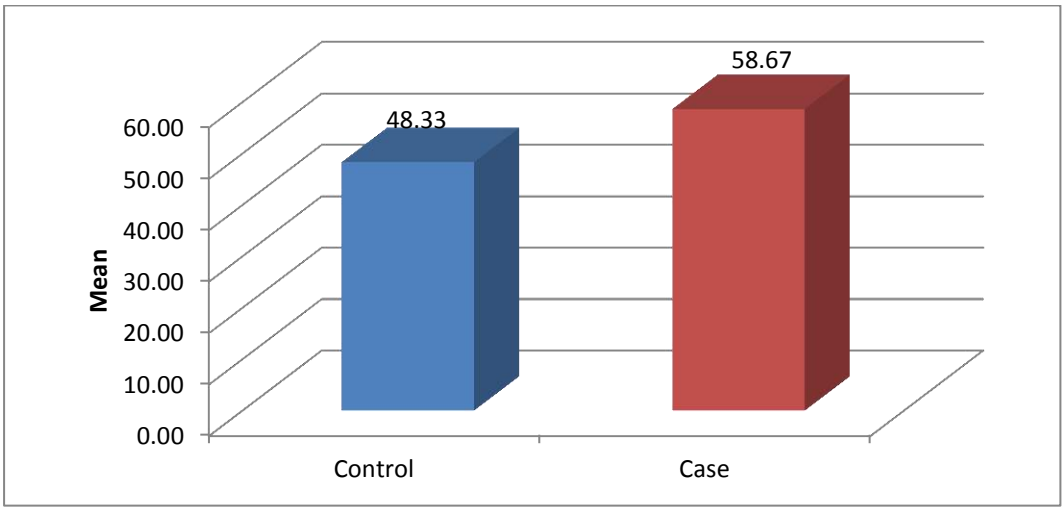


FIGURE 47: COMPARISON OF MEAN BMD OF TOTAL HIP OF CKD3

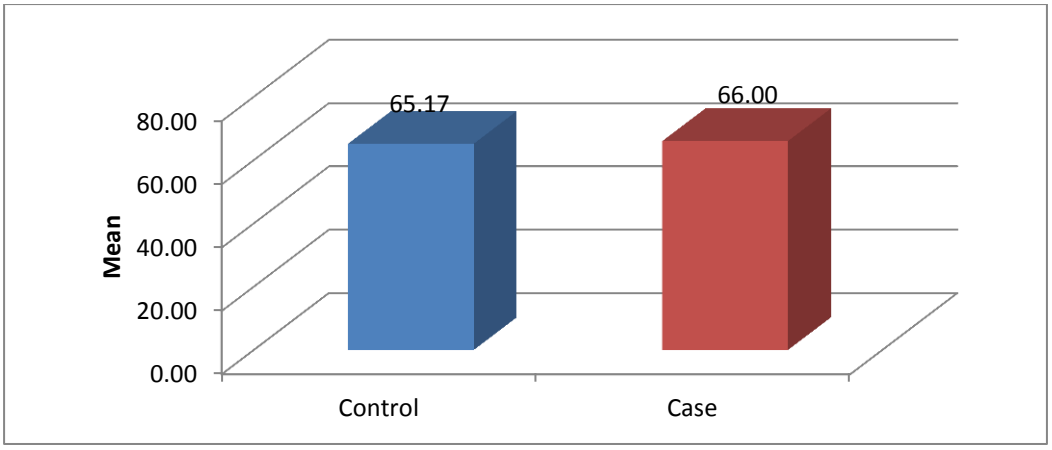
TABLE 48: COMPARISON OF BASELINE DEMOGRAPHIC FEATURES OF CKD 4

CKD 4 stage	Control		Case		t	P value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Age	48.33	11.00	58.67	5.16	-2.082	0.064	-10.33	4.96
Weight in Kg	65.17	6.08	66.00	9.67	-0.179	0.862	-0.83	4.66
Height in cm	164.50	4.85	167.50	1.64	-1.436	0.182	-3.00	2.09
SBP	125.67	8.04	131.00	6.03	-1.299	0.223	-5.33	4.10
DBP	81.33	4.32	81.00	2.45	0.164	0.873	0.33	2.03

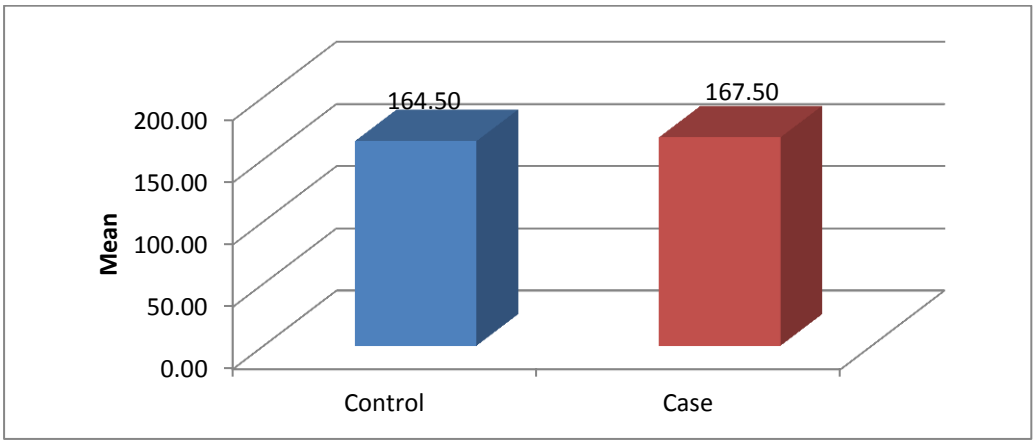
Mean age of control and case group was48.33 (SD=11.00) and 58.67 (SD=5.16) respectively. There was no statistically difference between two groups.



Mean weight of control and case group was 65.17 (SD=6.08) and 66.00 (SD=9.67) respectively. There was no statistically difference between two groups.



Mean height of control and case group was 164.50 (SD=4.85) and 167.50 (SD=1.64) respectively. There was no statistically difference between two groups.



Mean SBP for control and case group was125.67 (SD= 8.04) and 131.00 (SD= 6.03) respectively. Mean DBP for control and case group was 81.33 (SD= 4.32) and 81.00 (SD= 2.45) respectively.

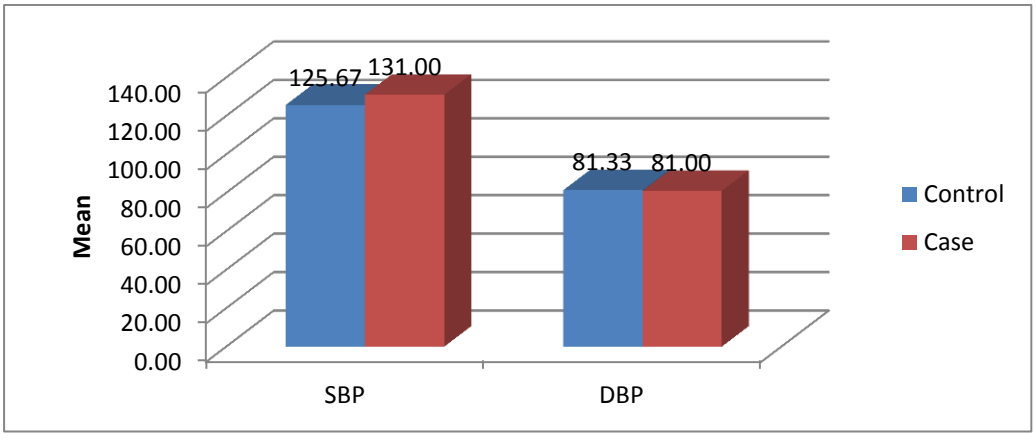


FIGURE 48: COMPARISON OF BASELINE DEMOGRAPHIC FEATURES OF CKD 4

TABLE 49: COMPARISON OF BASELINE COMPLETE BLOOD COUNTS OF CKD 4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Hemoglobin baseline g/dl	9.28	0.61	9.28	0.56	0.000	1.000	0.00	0.34
TLC baseline per ul	8.23	2.07	8.47	2.05	-0.196	0.848	-0.23	1.19
Platelets at baseline lakh	1.48	0.18	1.57	0.28	-0.690	0.506	-0.09	0.14

Baseline mean hemoglobin was 9.28 (SD= 0.61) and 9.28 (SD= 0.56) for control and case group respectively. Baseline TLC was 8.23 (SD=2.07) and 8.47(SD=2.05) for control and case group respectively. Baseline platelet count was 1.48 (SD=0.18) and 1.57(SD=0.28) for control and case group respectively.

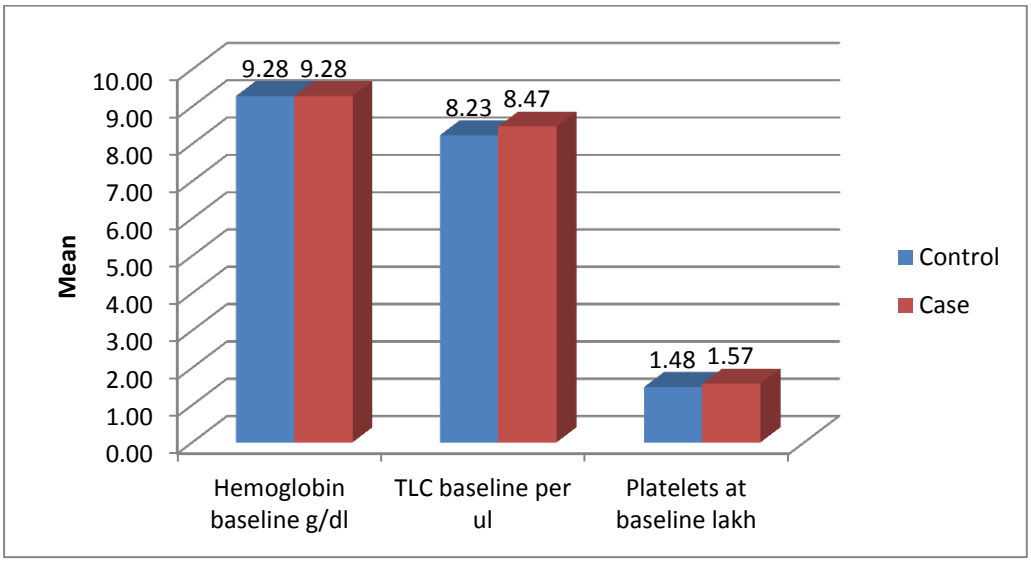


FIGURE 49: COMPARISON OF BASELINE COMPLETE BLOOD COUNTS OF CKD4

TABLE 50: COMPARISON OF THE MEAN UREA AND CREATININEAT BASELINEOF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Urea at baseline mg/dl	141.00	15.74	128.50	9.01	1.689	0.122	12.50	7.40
Creatinine baseline mg/dl	4.08	0.56	4.20	1.01	-0.247	0.810	-0.12	0.47

Baseline mean urea was 141.00 (SD= 15.74) and 128.50(SD= 9.01) for control and case group respectively. Baseline mean creatinine was 4.08 (SD= 0.56) and 4.20 (SD= 1.01) for control and case group respectively.

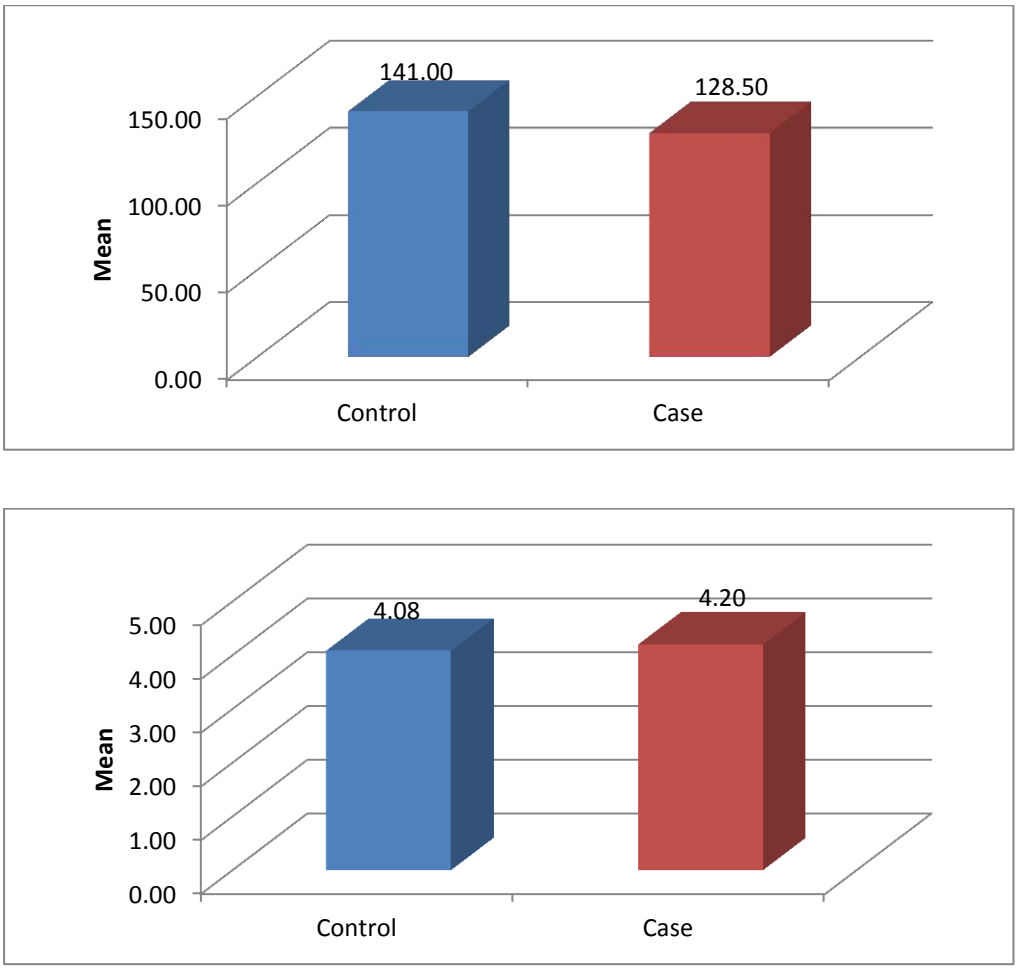


FIGURE 50: COMPARISON OF THE MEAN UREA AND CREATININEAT BASELINEOF CKD4

TABLE 51: COMPARISON OF THE MEAN SODIUM AND POTASSIUM AT BASELINEOF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Sodium baseline meq/l	136.67	7.92	134.83	4.12	0.503	0.626	1.83	3.64
Potassium at baseline meq/l	4.62	1.02	4.08	1.41	0.751	0.470	0.53	0.71

Baseline mean sodium was 136.67(SD= 7.92) and134.83 (SD= 4.12) for control and case group respectively. Baseline mean ptassium was 4.62 (SD= 1.02) and 4.08(SD= 1.41) for control and case group respectively.

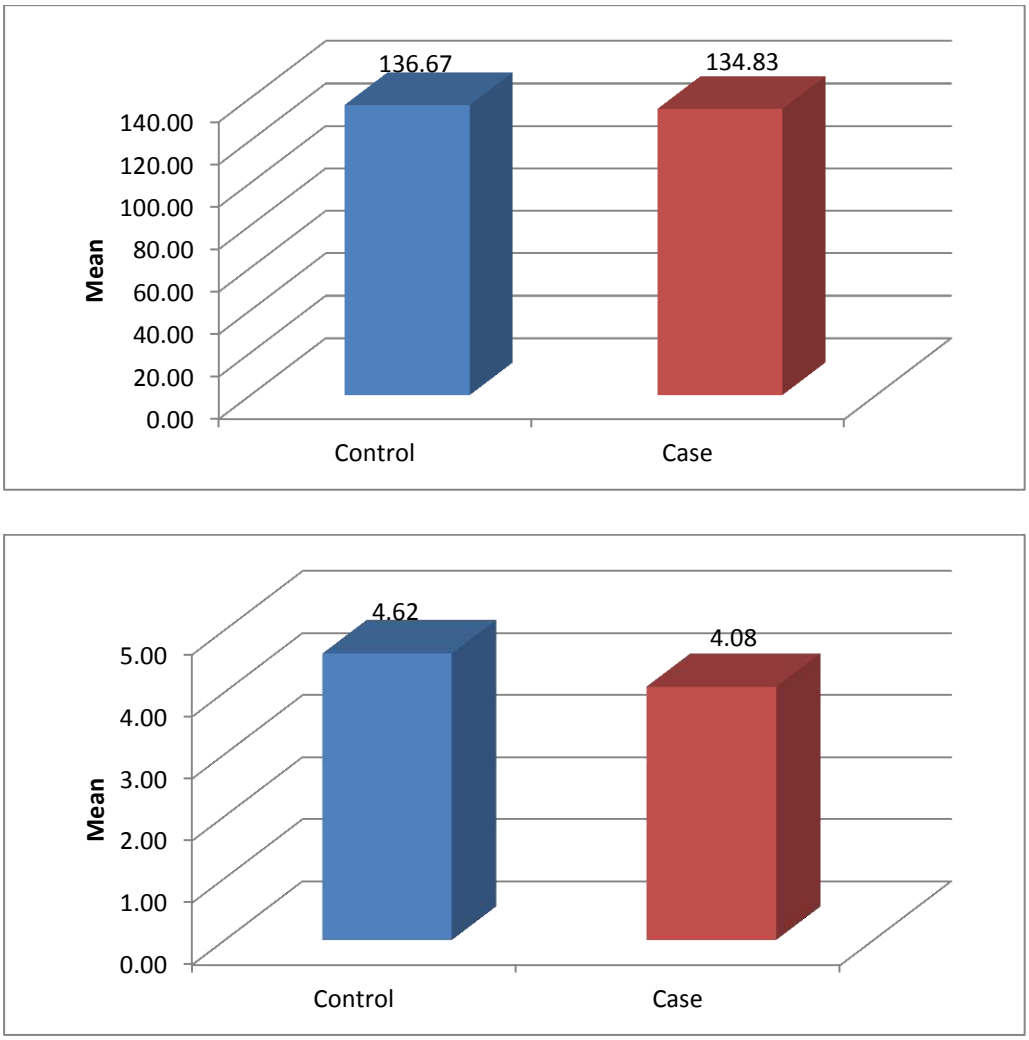


FIGURE 51: COMPARISON OF THE MEAN SODIUM AND POTASSIUM AT BASELINE OF CKD4

TABLE 52: COMPARISON OF THE MEAN CREATININE OF CKD4

CKD 4 stage	control		case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Creatinine baseline mg/dl	4.08	0.56	4.20	1.01	-0.247	0.810	-0.12	0.47
Creatinine at 3 months	5.30	1.36	4.93	1.42	0.457	0.657	0.37	0.80
creatinine at 6 months	5.68	1.31	4.53	1.02	1.692	0.122	1.15	0.68
creatinine at 12 months	5.23	1.35	4.95	0.98	0.417	0.685	0.28	0.68

Mean creatinine values were 4.08 (SD=0.56), 5.30 (SD=1.36), 5.68 (SD=1.31) and 5.23 (1.35) at baseline, 3 months, 6months and 12 months respectively in control group. Mean creatinine values were 4.20 (SD=1.01), 4.93 (SD=1.42), 4.53 (SD=1.02) and 4.95 (0.98) at baseline, 3 months, 6months and 12 months respectively in case group.

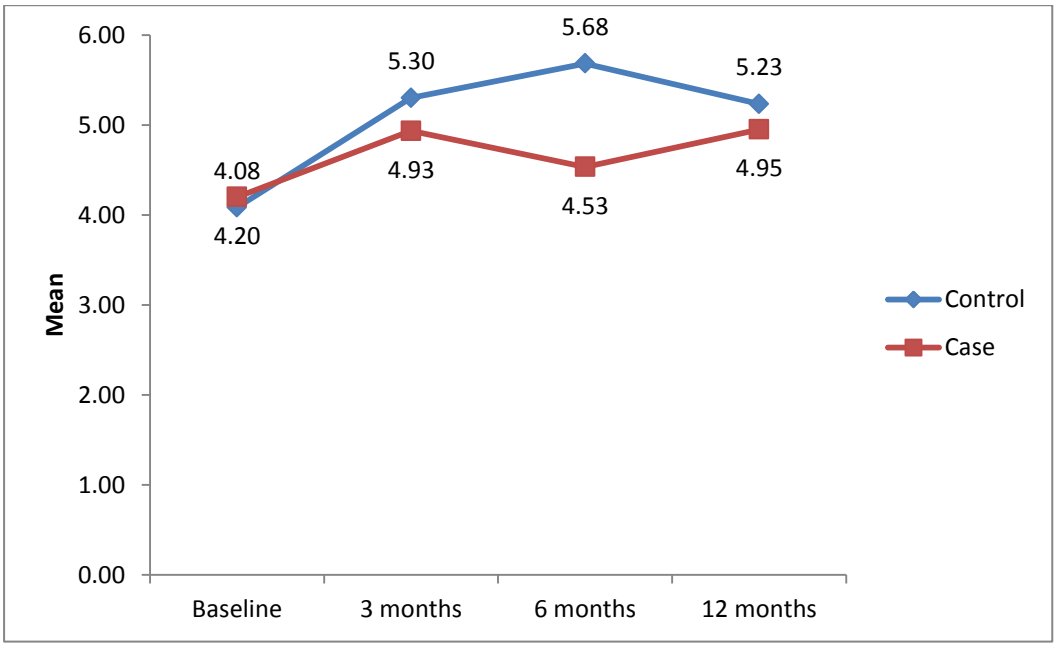


FIGURE 52: COMPARISON OF THE MEAN CREATININE OF CKD4

TABLE 53a: COMPARISON BETWEEN DIFFERENCE OF MEAN CREATININE OF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 3m	-1.22	1.37	-0.73	0.69	-0.771	0.459	-0.48	0.63
0- 6m	-1.60	1.42	-0.33	0.88	-1.861	0.092	-1.27	0.68
0- 12m	-1.15	0.98	-0.75	0.71	-0.808	0.438	-0.40	0.49
3-6m	-0.38	1.22	0.40	1.02	-1.204	0.256	-0.78	0.65
3-12m	0.07	1.79	-0.02	0.80	0.104	0.919	0.08	0.80
6-12m	0.45	1.93	-0.42	0.72	1.033	0.326	0.87	0.84

There was statistically no difference in change in the mean value of creatinine at 3, 6 and 12 months between control and case group. This was -0.38, 0.07, 0.45 at 3, 6 and 12 months for controls. This was 0.40, -0.02, -0.42 at 3, 6 and 12 months for cases.

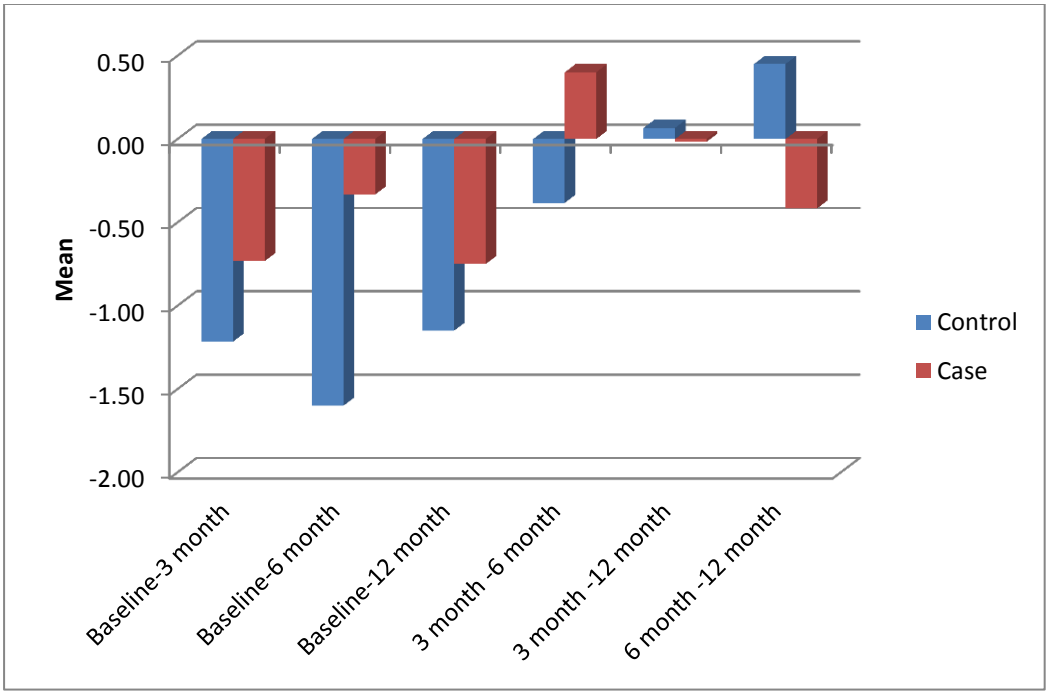


FIGURE 53a: COMPARISON BETWEEN DIFFERENCES OF MEAN CREATININE OF CKD4

TABLE 53b: PROGRESSION OF CKD4 TO CKD5

	Control	Case
Number	2	2
Percentage %	28.5	28.5

Total four patients, two each from case and control progressed from CKD4 to CKD5 stage at the end of one year.

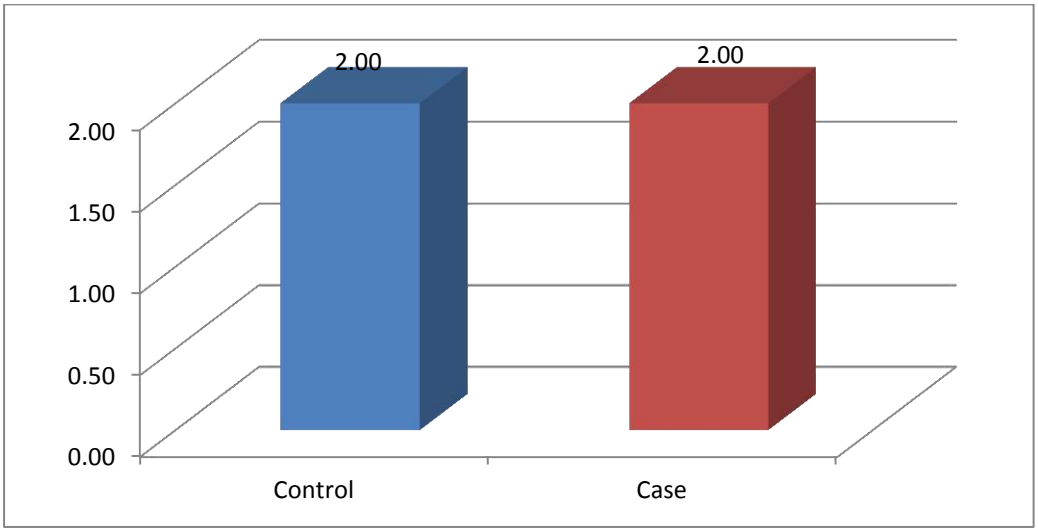


FIGURE 53b: PROGRESSION OF CKD4 TO CKD5

TABLE 53c: COMPARISON OF MEAN e GFR FOR CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
e GFR baseline	15.83	0.98	18.17	3.76	-1.469	0.173	-2.33	1.59
e GFR at 12 months	14.50	1.64	15.50	2.43	-0.835	0.423	-1.00	1.20

There was no significant difference in mean e GFR between two groups at end of 12 months.

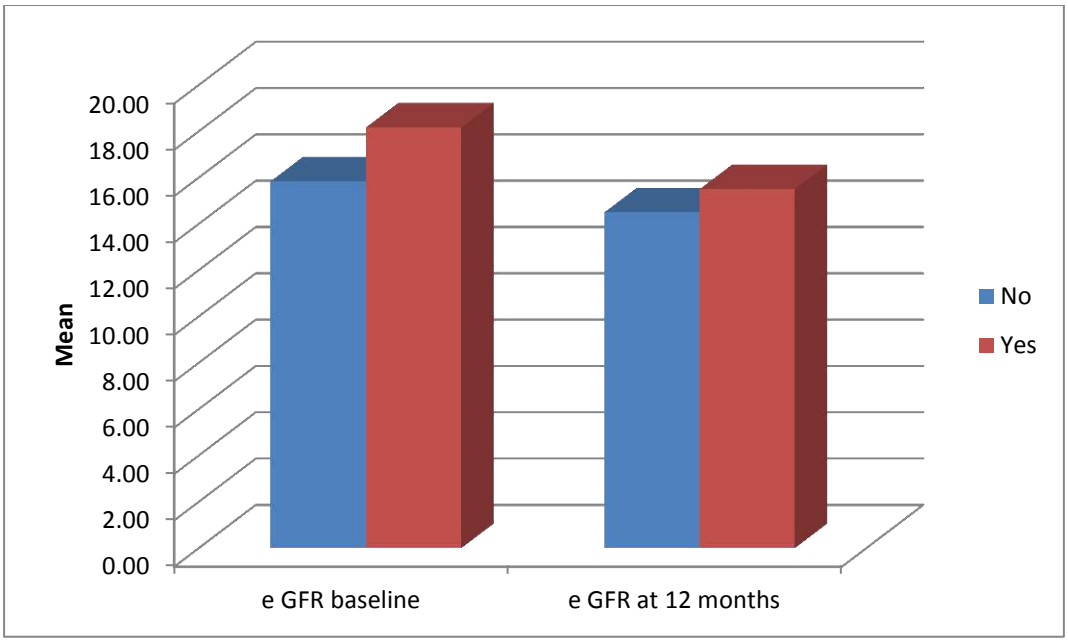


FIGURE 53c: COMPARISON OF MEAN eGFR FOR CKD4

TABLE 54: COMPARISON OF THE MEAN SERUM CALCIUM VALUE OF CKD4

CKD4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Calcium baseline mg/dl	8.98	0.82	8.30	0.72	1.535	0.156	0.68	0.45
calcium at 3 months	8.37	0.71	8.52	0.17	-0.500	0.628	-0.15	0.30
calcium at 6 months	8.33	0.43	8.85	0.72	-1.511	0.162	-0.52	0.34
calcium at 12 months	8.45	0.23	8.43	0.56	0.068	0.947	0.02	0.25

There was no difference in mean calcium level at baseline, 3, 6 and 12 months between control and case group. This was 8.88, 8.37, 8.33, 8.45, at baseline, 3, 6 and 12 months for controls. This was 8.30, 8.52, 8.85, 8.43 at baseline, 3, 6 and 12 months for cases.

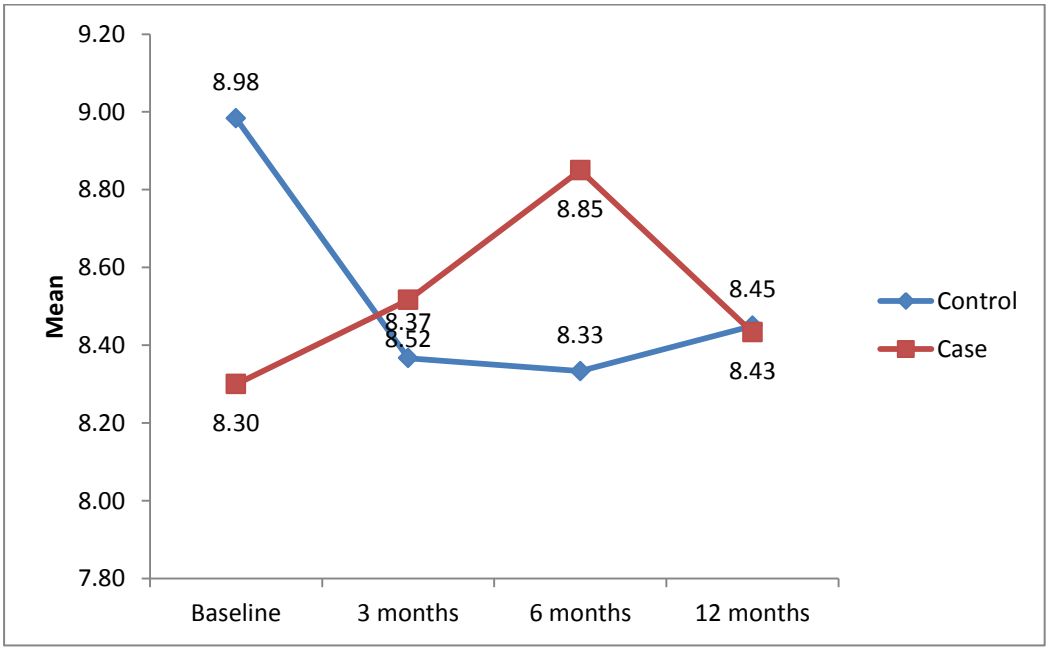


FIGURE 54: COMPARISON OF THE MEAN SERUM CALCIUM VALUE OF CKD4

TABLE 55: COMPARISON OF THE MEAN SERUM PHOSPHORUS VALUE OF CKD4

CKD4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Phosphorus mg/dl baseline	7.02	0.93	6.78	1.89	0.272	0.791	0.23	0.86
Phosphorus at 3 months	6.65	0.65	6.40	0.56	0.714	0.491	0.25	0.35
Phosphorus at 6 months	6.23	0.73	6.38	0.72	-0.359	0.727	-0.15	0.42
Phosphorus at 12 months	6.27	0.56	7.05	1.05	-1.616	0.137	-0.78	0.48

There was no difference in mean phosphorus level at baseline, 3, 6 and 12 months between control and case group. This was 7.02, 6.65, 6.23, 6.27 at baseline, 3, 6 and 12 months for controls. This was 6.78, 6.40, 6.38, 7.05 at baseline, 3, 6 and 12 months for cases.

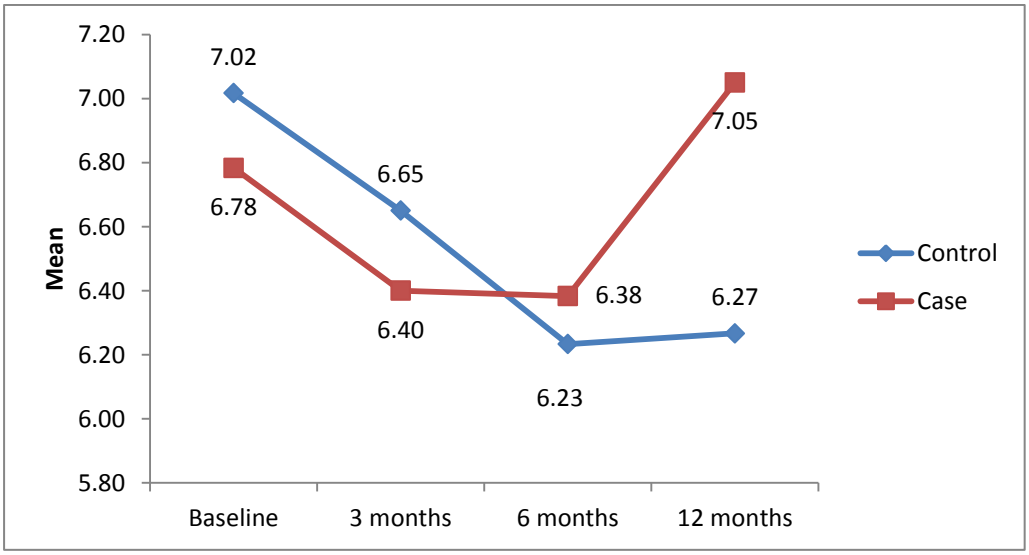


FIGURE 55: COMPARISON OF THE MEAN SERUM PHOSPHORUS VALUE OF CKD4

TABLE 56: COMPARISON OF THE MEAN SERUM ALKALINE PHOSPHATASE VALUE OF CKD4

CKD4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
ALP base line U/dl	153.83	13.76	146.17	11.37	1.052	0.318	7.67	7.29
ALP at 3 months	147.33	10.75	148.33	12.09	-0.151	0.883	-1.00	6.60
ALP at 6 months	151.67	14.38	151.67	12.50	0.000	1.000	0.00	7.78
ALP at 12 months	149.50	9.95	138.83	10.17	1.836	0.096	10.67	5.81

There was no difference in mean ALP level at baseline, 3, 6 and 12 months between control and case group. This was 153.83, 147.33, 15.67, 149.50 at baseline, 3, 6 and 12 months for controls. This was 146.17, 148.83, 151.67, 138.83 at baseline, 3, 6 and 12 months for cases.

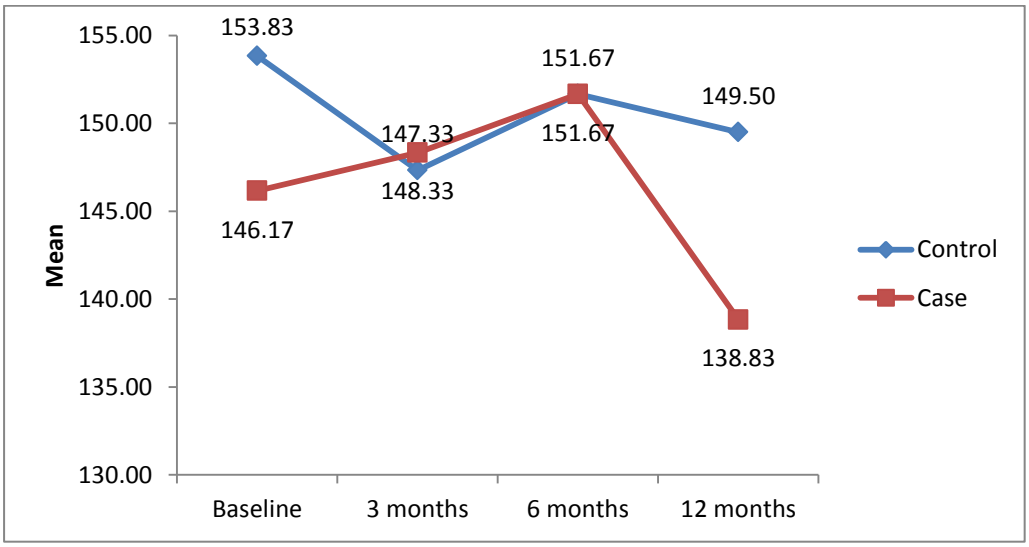


FIGURE 56: COMPARISON OF THE MEAN SERUM ALKALINE PHOSPHATASE VALUE OF CKD4

TABLE 57: COMPARISON OF THE MEAN PTH VALUES OF CKD4

CKD4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
IPTH pg/ml baseline	193.50	18.22	195.17	16.56	-0.166	0.872	-1.67	10.05
iPTH at 3 months	190.67	9.46	191.33	9.33	-0.123	0.905	-0.67	5.42
iPTH at 6 months	183.83	13.72	195.83	11.81	-1.624	0.135	-12.00	7.39
iPTH at 12 months	183.50	18.64	174.67	11.31	0.992	0.344	8.83	8.90

There was no difference in mean PTH level at baseline, 3, 6 and 12 months between control and case groups of CKD4. PTH values were193.50, 190.67, 183.83, 183.50, at baseline, 3, 6 and 12 months for controls. These were195.17, 191.33, 195.83, 174.67 at baseline, 3, 6 and 12 months for cases. But there was statistically significance difference in change mean PTH level between control and cases at 6 and 12 months.

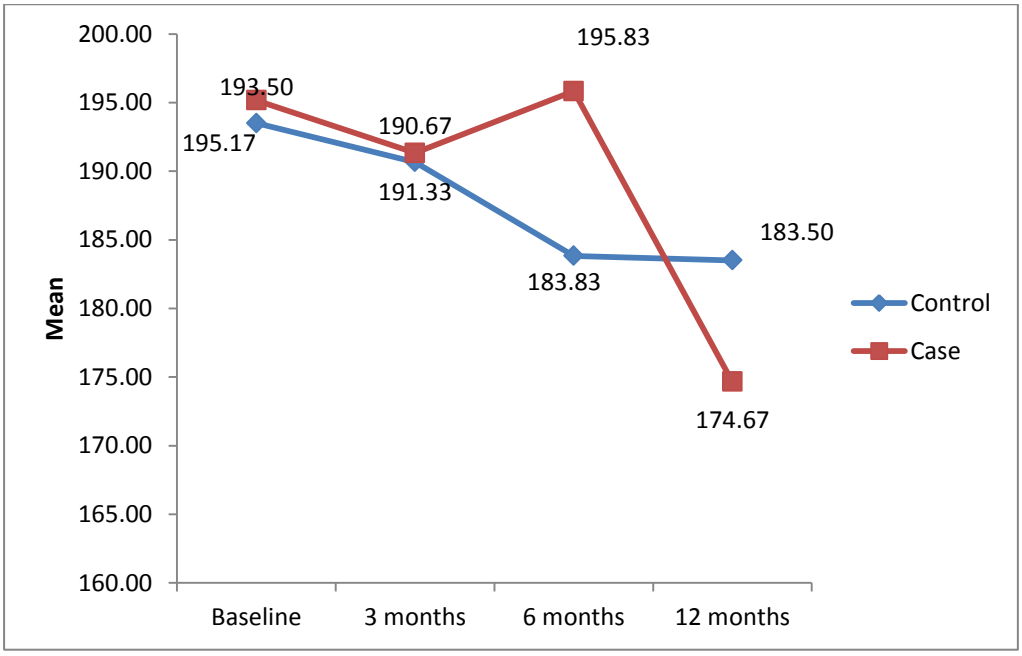


FIGURE 57: COMPARISON OF THE MEAN PTH VALUES OF CKD4

TABLE 58: COMPARISON OF DIFFERENCE IN MEAN PTH VALUE OF CKD4

CKD4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-3m	2.83	11.11	3.83	8.52	-0.175	0.865	-1.00	5.71
0-6m	9.67	16.80	-0.67	11.57	1.241	0.243	10.33	8.33
0-12m	10.00	29.28	20.50	17.17	-0.758	0.466	-10.50	13.86
3-6m	6.83	10.34	-4.50	6.22	2.300	0.044	11.33	4.93
3-12m	7.17	22.52	16.67	11.84	-0.915	0.382	-9.50	10.39
6-12m	0.33	18.86	21.17	9.91	-2.395	0.038	-20.83	8.70

There was statistically significant difference in change in the mean value of PTH at 6 month when compared to 3 month and at 12 month when compared to 6 month between control and case group.

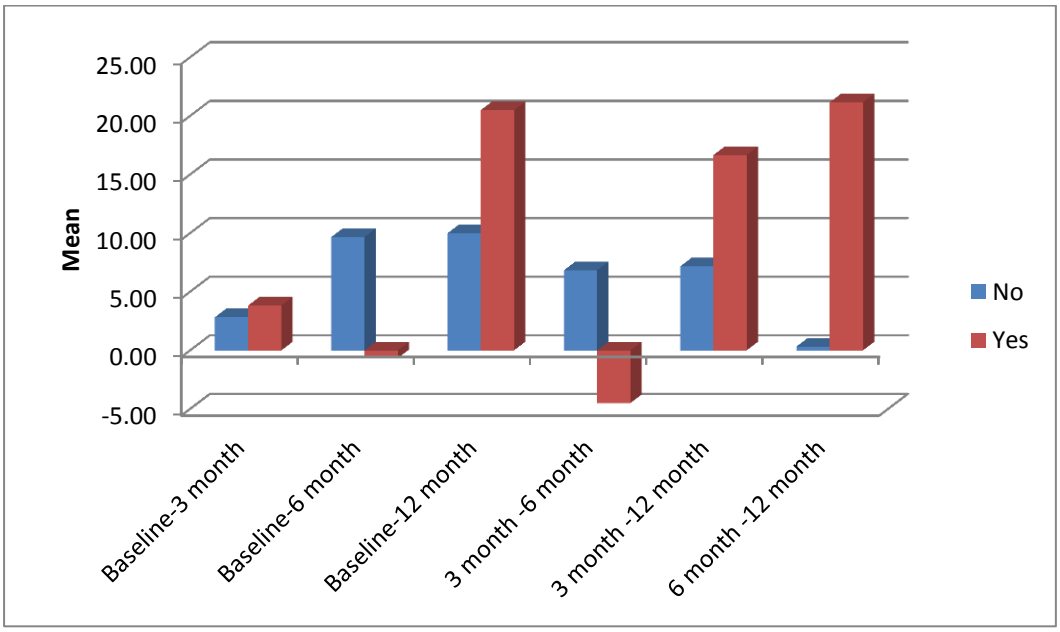


FIGURE 58: COMPARISON OF DIFFERENCE IN MEAN PTH VALUE OF CKD4

TABLE 59: COMPARISON OF THE MEAN VITAMIN D3 VALUES OF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Vitamin D3 ng/ml baseline	25.83	2.32	24.00	2.53	1.309	0.220	1.83	1.40
Vitamin D3 at 3 months	26.17	3.87	25.67	2.16	0.276	0.788	0.50	1.81
Vitamin D3 at 6 months	27.83	2.56	27.33	1.75	0.395	0.701	0.50	1.27
Vitamin D3 at 12 months	25.50	1.64	25.83	3.06	-0.235	0.819	-0.33	1.42

There was no difference in mean vitamin D3 level at baseline, 3, 6 and 12 months between control and case group. This was 25.83, 26.17, 27.83, 25.50 at baseline, 3, 6 and 12 months for controls. This was 24.00, 25.67, 27.33, 25.83 at baseline, 3, 6 and 12 months for cases.

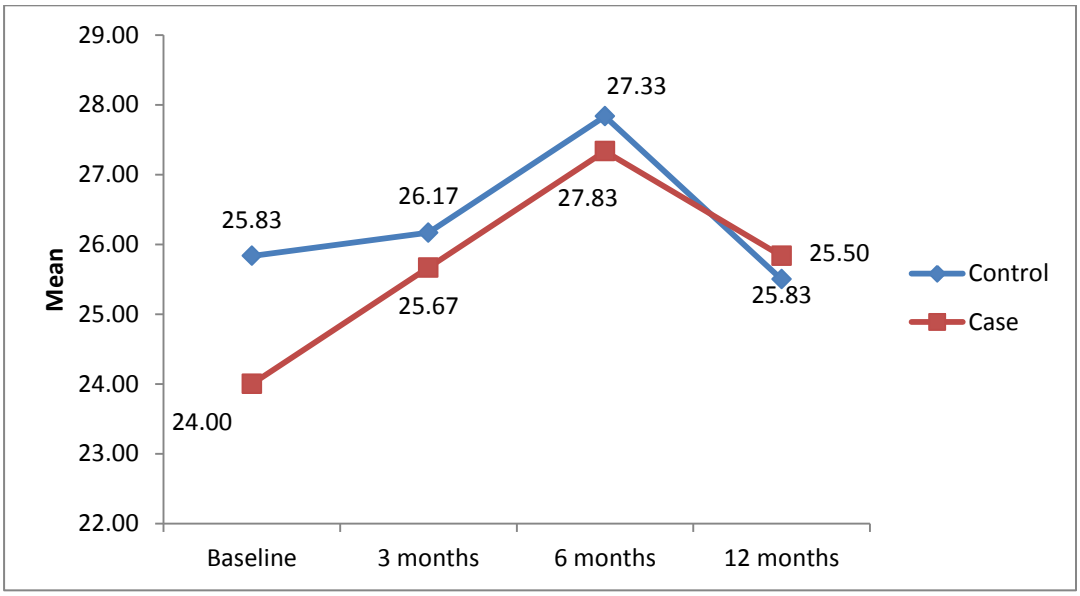


FIGURE 59: COMPARISON OF THE MEAN VITAMIN D3 VALUES OF CKD4

TABLE 60: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF LUMBAR SPINE OF CKD4

CKD4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6M	0.10	0.06	-0.15	0.12	4.443	0.001	0.25	0.06
0-12M	0.28	0.12	-0.35	0.23	6.101	0.000	0.63	0.10

Mean lumbar spine T score was -1.72 for case and -0.38 for control respectively at baseline. It was -1.57 and -0.48 for case and control respectively at 6 months. It was -1.37 and -0.67 or case and control respectively at 12 months. There was improvement in mean T score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of T score was statistically significant between two groups at 6 and 12 month.

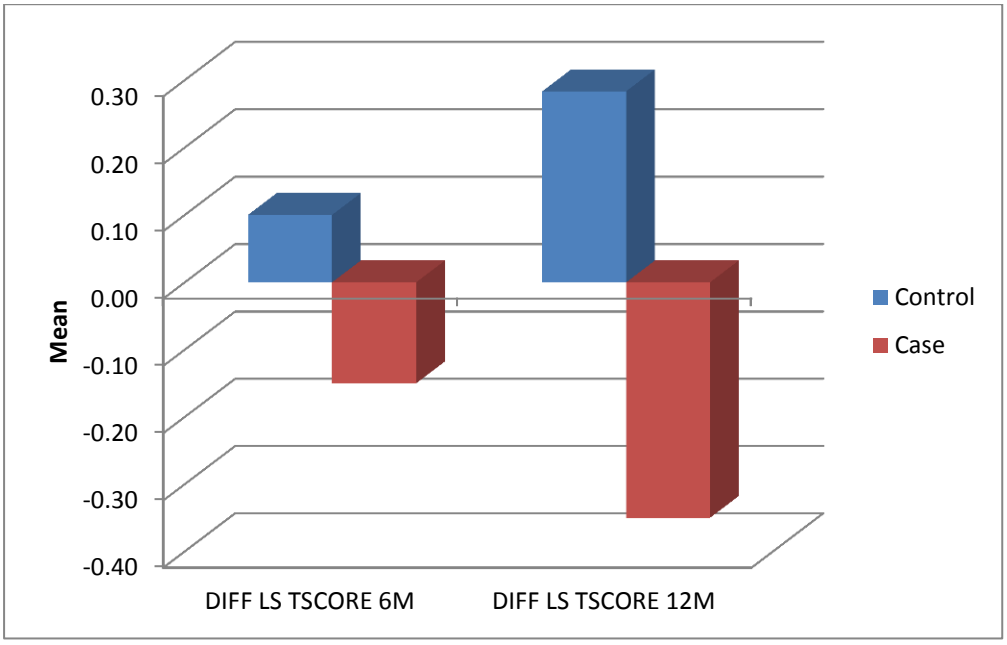


FIGURE 60: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF LUMBAR SPINE OF CKD 4

TABLE 61: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF LUMBAR SPINE OF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6M	0.12	0.12	-0.12	0.04	4.616	0.001	0.23	0.05
0- 12M	0.17	0.10	-0.27	0.10	7.281	0.000	0.43	0.06

Mean lumbar spine Z score was -0.63 for case and 0.02 for control respectively at baseline. It was -0.62 and -0.10 for case and control respectively at 6 months. It was -0.37 and -0.15for case and control respectively at 12 months.

There was improvement in mean Z score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of Z score was statistically significant between 2 groups at 6 and 12 month.

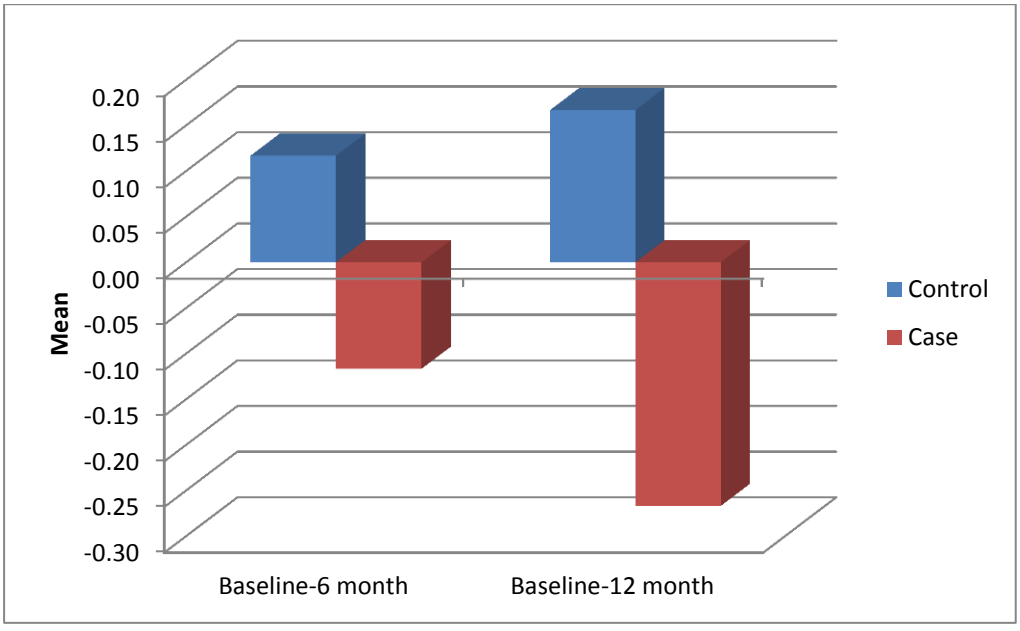


FIGURE 61: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF LUMBAR SPINE OF CKD4

TABLE 62: COMPARISON OF MEAN BMD AT LEVEL OF LUMBAR SPINE OF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline g/m2	1.28	0.32	1.02	0.16	1.757	0.109	0.26	0.15
At 6 month	1.24	0.34	1.07	0.19	1.083	0.304	0.17	0.16
At 12month	1.16	0.33	1.15	0.20	0.053	0.959	0.01	0.16
DIFFERENCE 0-6M	0.04	0.03	-0.04	0.03	5.058	0.000	0.09	0.02
DIFFERENCE 0-12M	0.12	0.04	-0.13	0.05	10.196	0.000	0.25	0.02

Mean lumbar spine BMD was 1.02 for case and 1.28 for control respectively at baseline. It was 1.07 and 1.24 for case and control respectively at 6 months. It was 1.15 and 1.16for case and control respectively at 12 month.

There was improvement in mean BMD at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in change in mean BMD was statistically significant between two groups at 6 and 12 month.

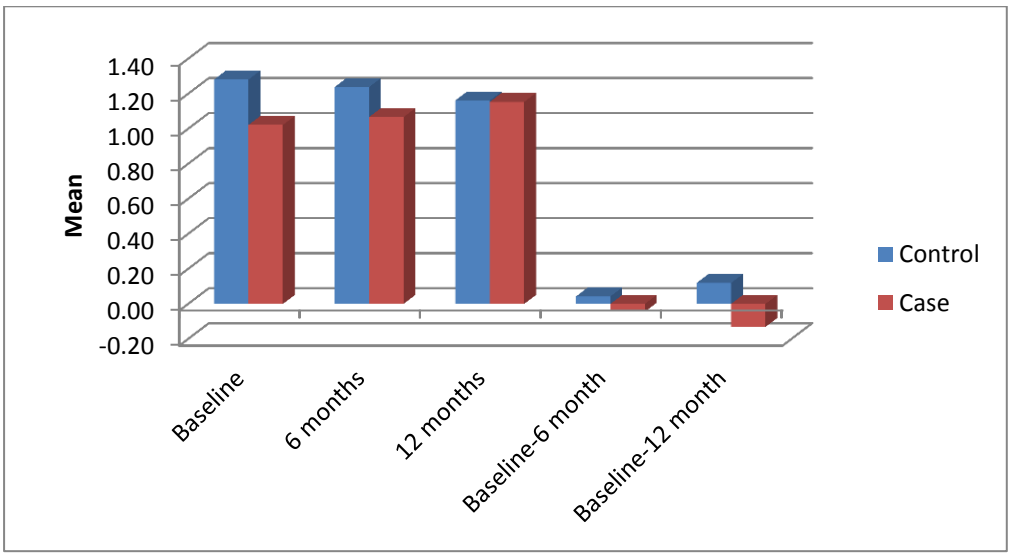


FIGURE 62: COMPARISON OF MEAN BMD AT LEVEL OF LUMBAR SPINE OF CKD4

TABLE 63: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF FEMUR NECK OF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6M	0.08	0.19	-0.28	0.40	2.012	0.072	0.37	0.18
0-12M	0.10	0.28	-0.37	0.41	2.302	0.044	0.47	0.20

Mean femur neck T score was -1.75 for case and -1.18 for control respectively at baseline. It was -1.47 and -1.27 for case and control respectively at 6 months. It was -1.38 and -1.28 for case and control respectively at 12 month.

There was improvement in mean T score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean T score was statistically significant between two groups at 6 and 12 month.

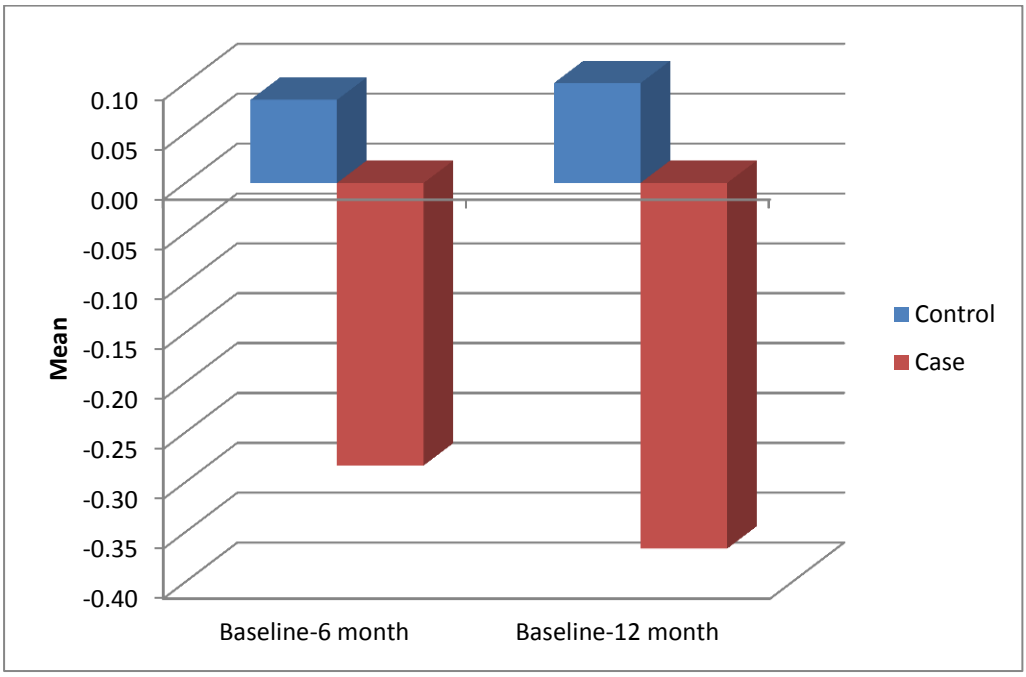


FIGURE 63: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF FEMUR NECK OF CKD4

TABLE 64: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF FEMUR NECK OF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6M	0.10	0.06	-0.15	0.08	5.839	0.000	0.25	0.04
0- 12M	0.22	0.13	-0.30	0.12	7.002	0.000	0.52	0.07

Mean femur neck Z score was -0.67 for case and 0.02 for control respectively at baseline. It was -0.52 and -0.08 for case and control respectively at 6 months. It was -0.37 and -0.20 for case and control respectively at 12 months.

There was improvement in mean Z score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean T score was statistically significant between two groups at 6 and 12 month.

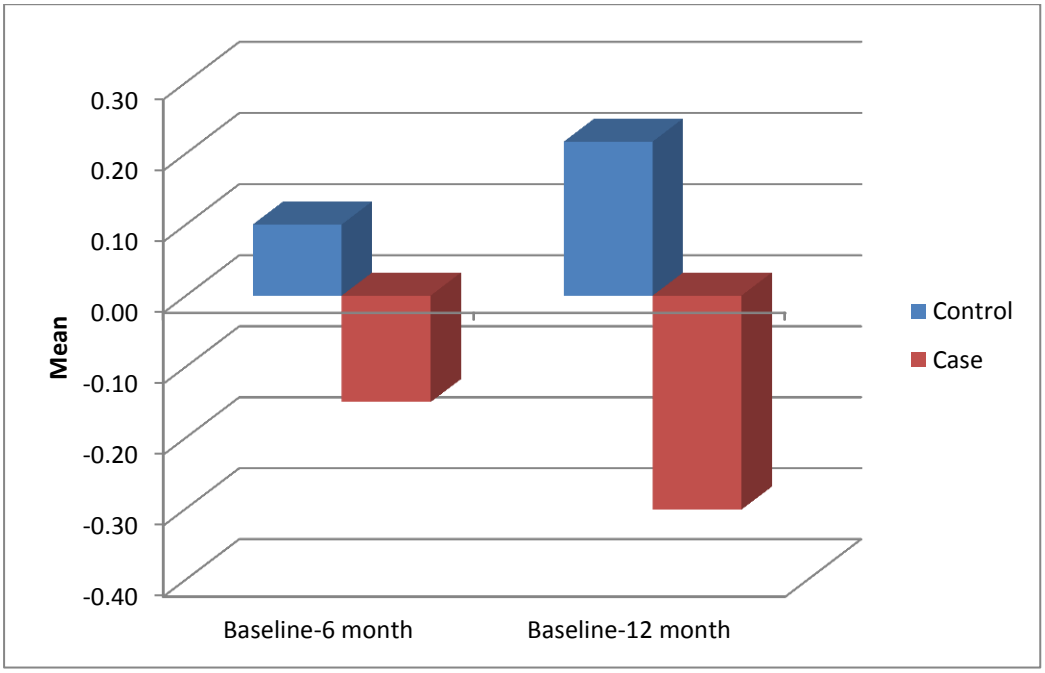


FIGURE 64: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF FEMUR NECK OF CKD4

TABLE 65: COMPARISON OF MEAN BMD AT LEVEL OF FEMUR NECK OF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline at femur neck	0.91	0.08	0.79	0.18	1.498	0.165	0.12	0.08
At 6 month	0.83	0.10	0.84	0.20	-0.147	0.886	-0.01	0.09
At 12 months	0.78	0.08	0.97	0.24	-1.891	0.088	-0.20	0.10
DIFFERENCE 0-6M	0.08	0.06	-0.05	0.05	4.257	0.002	0.14	0.03
DIFFERENCE 0-12M	0.14	0.06	-0.18	0.11	6.079	0.000	0.32	0.05

Mean femur neck BMD was 0.79 for case and 0.91 for control respectively at baseline. It was 0.84 and 0.83 for case and control respectively at 6 months. It was 0.97 and 0.78for case and control respectively at 12 month.

There was improvement in mean BMD at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in change mean BMD was statistically significant between two groups at 6 and 12 month.

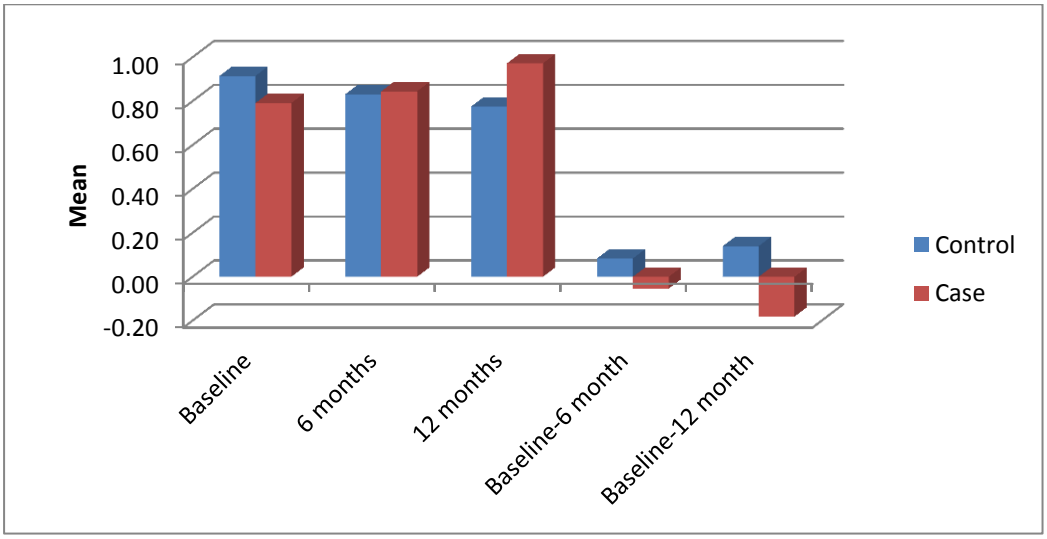


FIGURE 65: COMPARISON OF MEAN BMD AT LEVEL OF FEMUR NECKOF CKD4

TABLE 66: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE OF TOTAL HIP OF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6M	0.02	0.10	-0.25	0.16	3.411	0.007	0.27	0.08
0- 12M	0.02	0.13	-0.43	0.22	4.281	0.002	0.44	0.10

Mean total hip T score was -1.30 for case and -1.00 for control respectively at baseline. It was -1.05 and -1.02 for case and control respectively at 6 months. It was -0.87 and -1.02for case and control respectively at 12 month.

There was improvement in mean T score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in change in mean T score was statistically significant between two groups at 6 and 12 month.

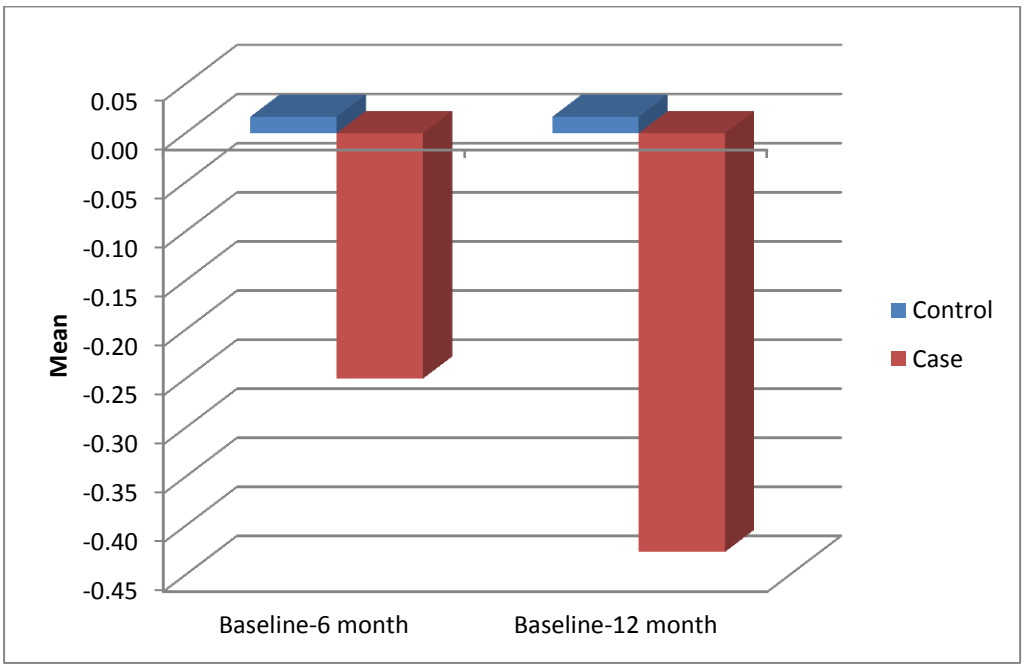


FIGURE 66: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE OF TOTAL HIP OF CKD4

TABLE 67: COMPARISON OFTHE DIFFERENCE OF MEAN Z SCORE OF TOTAL HIP OF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6M	0.02	0.08	-0.17	0.10	3.514	0.006	0.18	0.05
0-12M	-0.02	0.19	-0.32	0.17	2.832	0.018	0.30	0.11

Mean total hip Z score was -0.62 for case and -0.45 for control respectively at baseline. It was -0.45and -0.47 for case and control respectively at 6 months. It was -0.30 and -0.43 for case and control respectively at 12 months.

There was improvement in mean Z score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in change in mean Z score was statistically significant between two groups at 6 and 12 month.

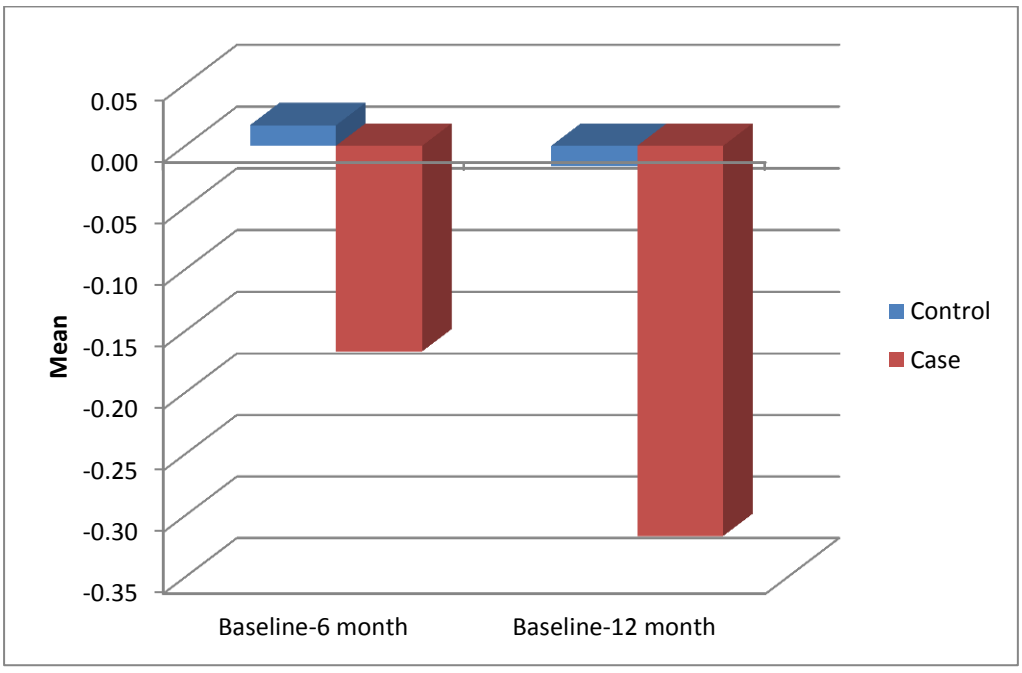


FIGURE 67: COMPARISON OFTHE DIFFERENCE OF MEAN Z SCORE OF TOTAL HIP OF CKD4

TABLE 68: COMPARISON OF MEAN BMD OF TOTAL HIP OF CKD4

CKD 4 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline	1.04	0.21	0.87	0.20	1.420	0.186	0.17	0.12
At 6 months	0.99	0.18	0.96	0.25	0.242	0.814	0.03	0.12
At 12 months	0.96	0.21	1.09	0.32	-0.862	0.409	-0.13	0.15
DIFFERENCE 0-6M	0.05	0.04	-0.09	0.08	3.771	0.004	0.14	0.04
DIFFERENCE 0-12M	0.08	0.05	-0.22	0.12	5.511	0.000	0.30	0.05

Mean total hip BMD was 0.87 for case and 1.04 for control respectively at baseline. It was 0.96 and 0.99 for case and control respectively at 6 months. It was 1.09 and 0.96 for case and control respectively at 12 month.

There was improvement in mean BMD at level of total hip at 6 and 12 month in patients, who received oral alendronate compared to controls. This difference in change in mean BMD was statistically significant between two groups at 6 and 12 month.

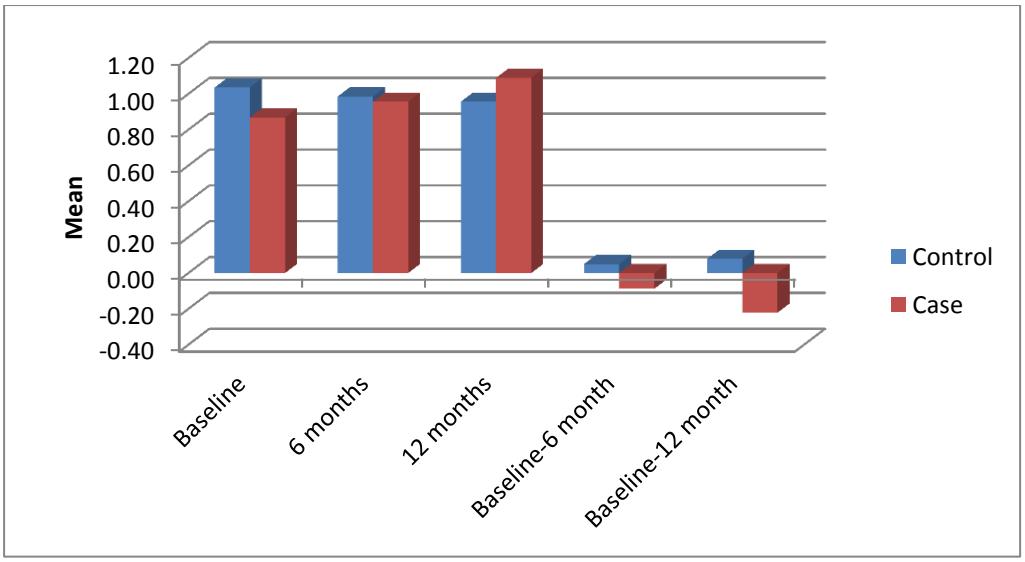
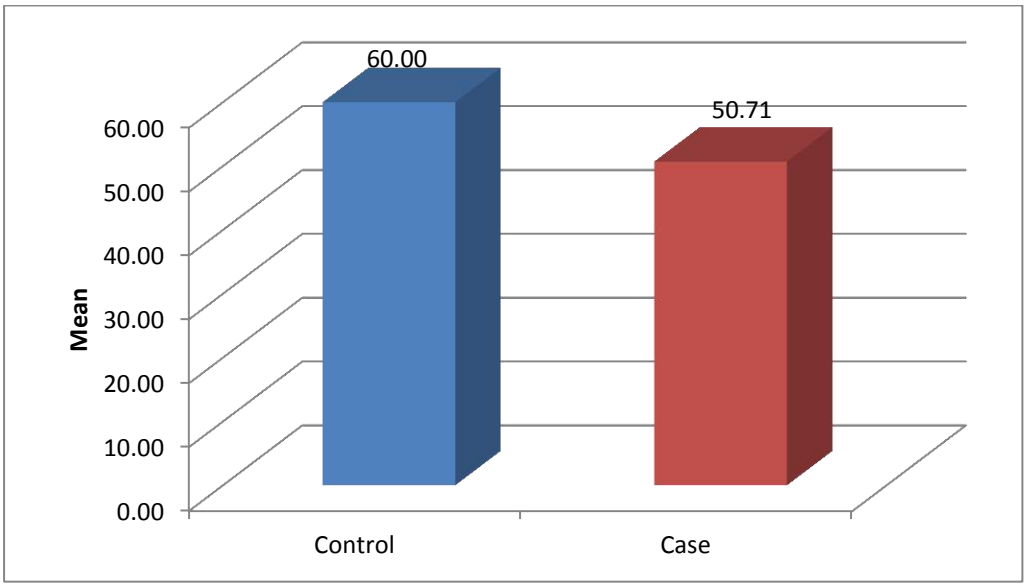


FIGURE 68: COMPARISON OF MEAN BMD OF TOTAL HIP OF CKD4

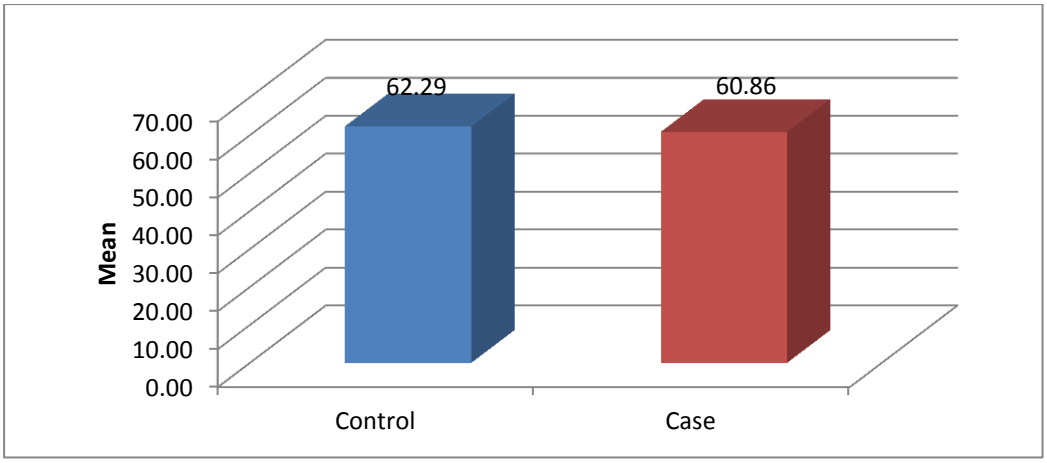
TABLE 69: COMPARISON OF BASELINE DEMOGRAPHIC FEATURES OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Age	60.00	7.85	50.71	14.63	1.480	0.165	9.29	6.27
Weight in Kg	62.29	4.23	60.86	5.08	0.572	0.578	1.43	2.50
Height in cm	167.14	2.41	168.14	1.77	-0.884	0.394	-1.00	1.13
SBP	128.29	4.68	126.86	7.01	0.448	0.662	1.43	3.19
DBP	80.29	5.09	80.00	5.77	0.098	0.923	0.29	2.91

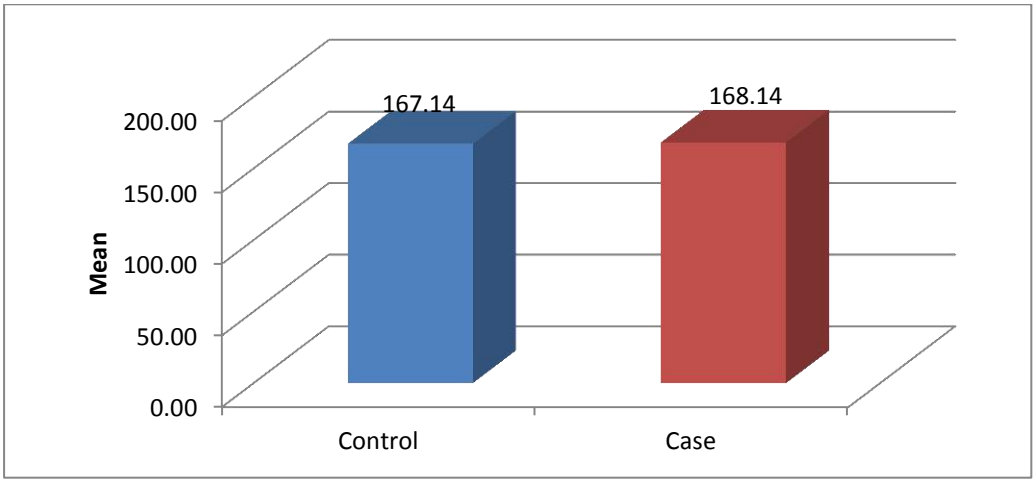
Mean age of control and case group was 60.00 (SD=7.85) and 50.71 (SD=14.63) respectively. There was statistically no difference between two groups.



Mean weight of control and case group was 62.29(SD=4.23) and 60.86(SD=5.08) respectively. There was statistically no difference between two groups.



Mean height of control and case group was 167.14 (SD=2.41) and 168.14 (SD=1.77) respectively. There was no statistically difference between two groups.



Mean SBP for control and case group was128.29 (SD= 4.68) and 126.86 (SD= 7.01) respectively. Mean DBP for control and case group was 80.29 (SD= 5.09) and 80.00 (SD= 5.77) respectively.

FIGURE 69: COMPARISON OF BASELINE DEMOGRAPHIC FEATURES OF CKD5

TABLE 70: COMPARISON OF BASELINE COMPLETE BLOOD COUNTS OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Hemoglobin baseline g/dl	9.57	0.61	9.26	0.58	0.993	0.341	0.31	0.32
TLC baseline per ul	8.63	2.13	8.91	1.75	-0.274	0.789	-0.29	1.04
Platelets at baseline lakh	1.66	0.36	1.68	0.27	-0.142	0.889	-0.02	0.17

Baseline mean hemoglobin was 9.57(SD= 0.61) and 9.26(SD= 0.58) for control and case group respectively. Baseline TLC was 8.63(SD=2.13) and 8.91(SD=1.75) for control and case group respectively. Baseline platelet count was 1.66 (SD=0.36) and 1.68(SD=0.27) for control and case group respectively.

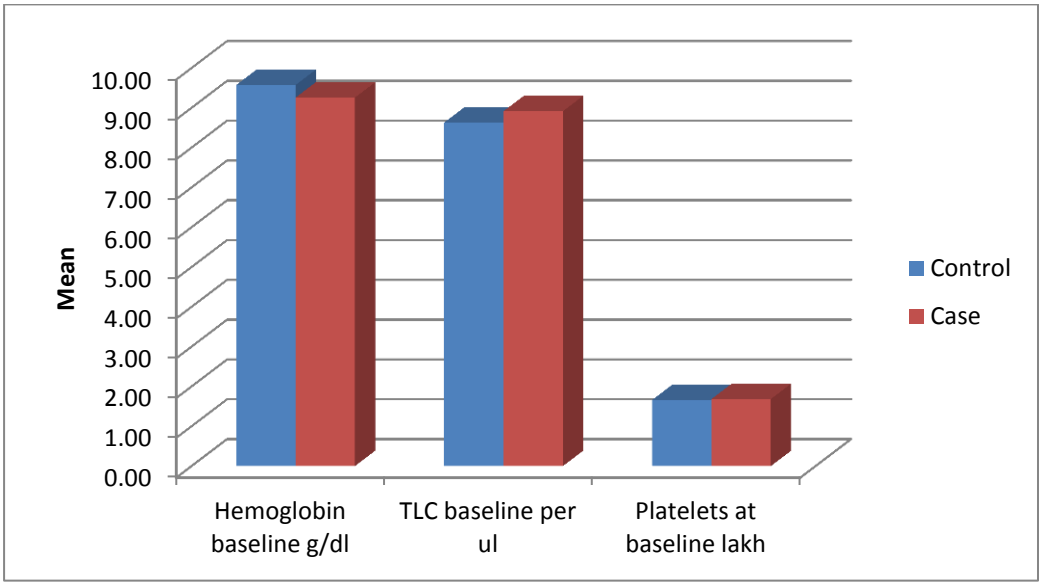


FIGURE 70: COMPARISON OF BASELINE COMPLETE BLOOD COUNTS OF CKD5

TABLE 71: COMPARISON OF THE MEAN UREA AND CREATININEAT BASELINEOF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Urea at baseline mg/dl	130.71	15.22	131.86	11.05	-0.161	0.875	-1.14	7.11
Creatinine baseline mg/dl	4.67	1.11	5.06	0.97	-0.693	0.502	-0.39	0.56

Baseline mean urea was 130.71(SD= 15.22) and 131.86(SD= 11.05) for control and case group respectively. Baseline mean creatinine was 4.67(SD= 1.11) and 5.06(SD= 0.97) for control and case group respectively.

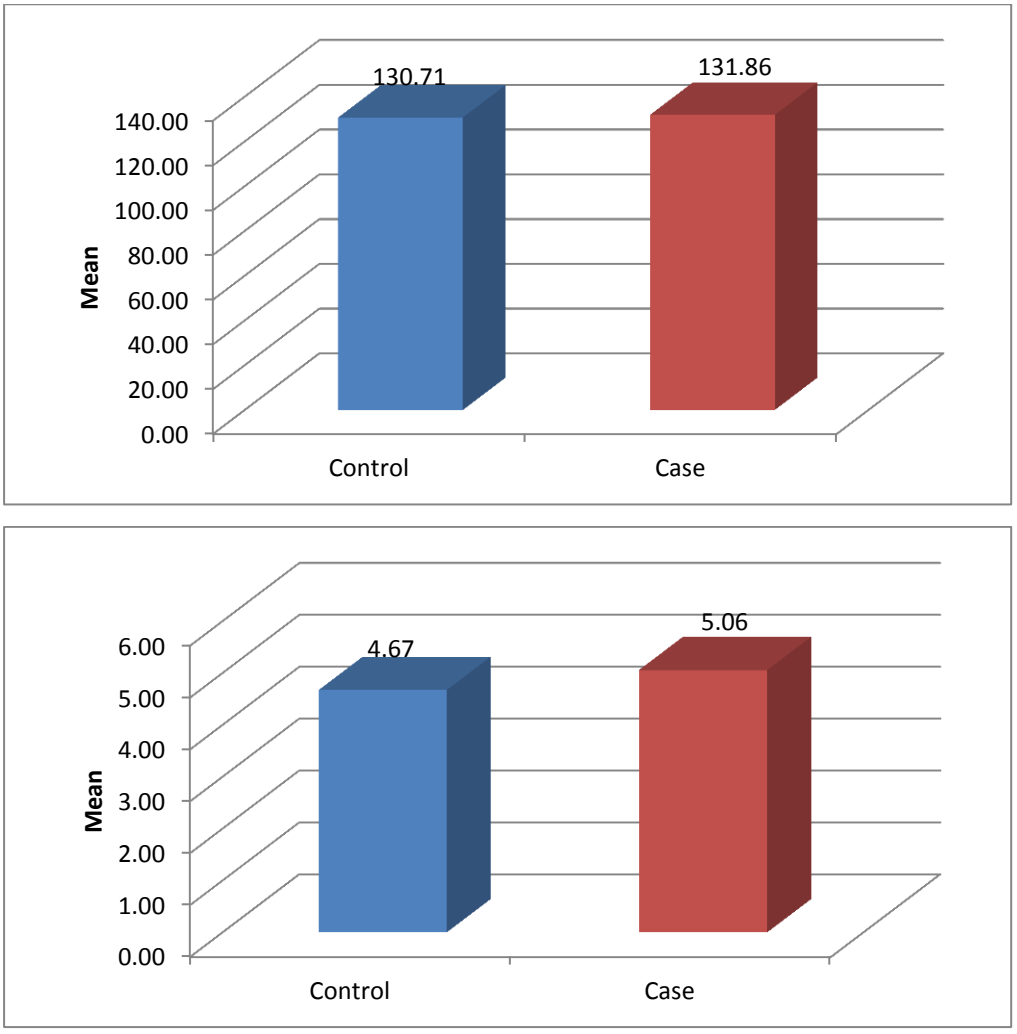


FIGURE 71: COMPARISON OF THE MEAN UREA AND CREATININEAT BASELINEOF CKD5

TABLE 72: COMPARISON OF THE MEAN SODIUM AND POTASSIUM AT BASELINEOF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Sodium baseline meq/l	135.57	2.64	135.71	5.94	-0.058	0.955	-0.14	2.46
Potassium at baseline meq/l	4.07	0.97	4.86	1.17	-1.369	0.196	-0.79	0.57

Baseline mean sodium was 135.57(SD= 2.64) and135.71(SD= 5.94) for control and case group respectively. Baseline mean ptassium was 4.07 (SD= 0.97) and 4.86(SD= 1.17) for control and case group respectively.

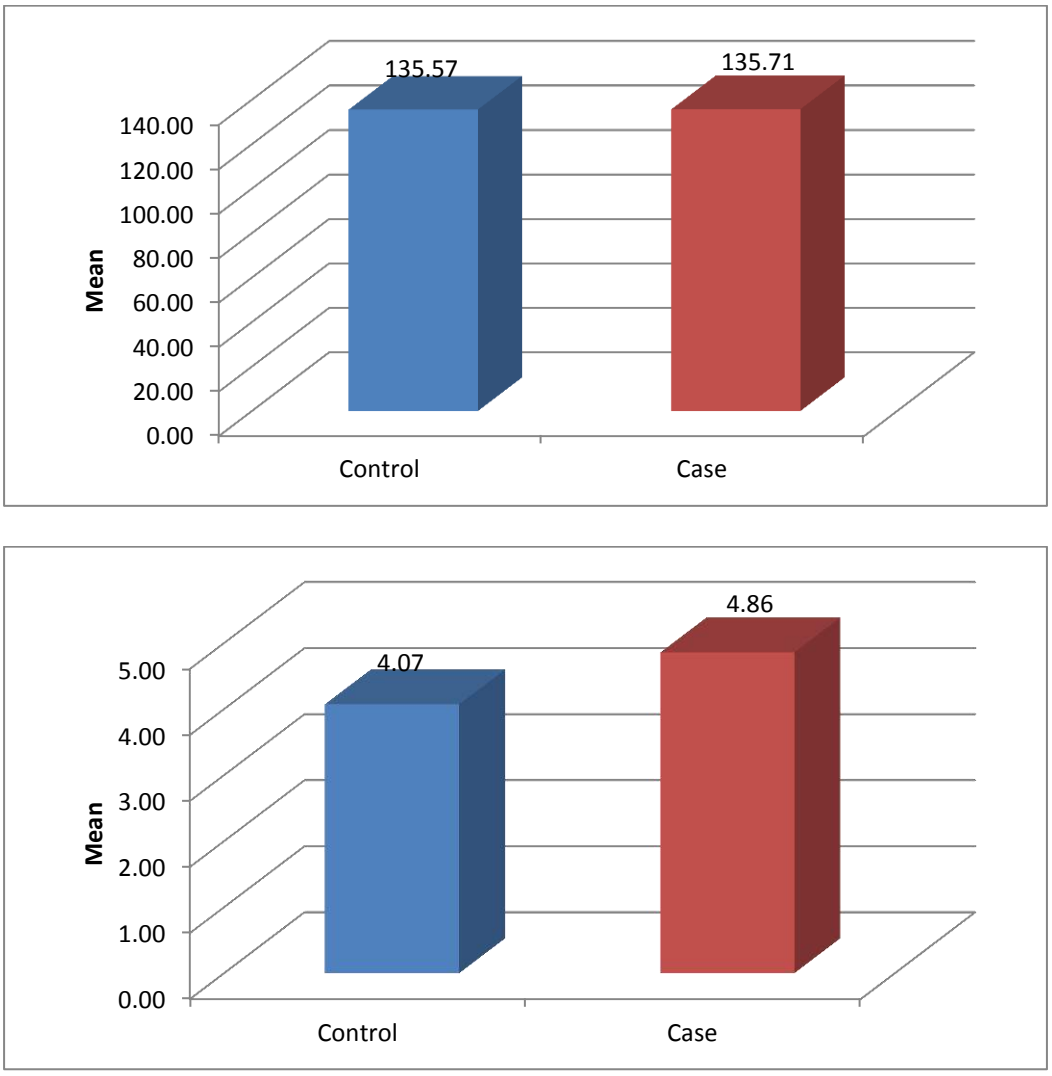


FIGURE 72: COMPARISON OF THE MEAN SODIUM AND POTASSIUM AT BASELINEOF CKD5

TABLE 73: COMPARISON OF THE MEAN CREATININE OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean mg/dl	SD	Mean	SD			Mean	SD
Baseline	4.67	1.11	5.06	0.97	-0.693	0.502	-0.39	0.56
At 3 month	4.97	0.86	5.54	0.99	-1.158	0.269	-0.57	0.49
At 6 month	5.91	0.81	5.39	1.30	0.916	0.378	0.53	0.58
At 12 month	6.07	0.73	6.20	0.97	-0.281	0.783	-0.13	0.46

Mean creatinine values were 4.67(SD=1.11), 4.97(SD=0.86), 5.54(SD=0.99) and 6.07 (0.73) at baseline, 3 months, 6 months and 12 months respectively in control group. Mean creatinine values were 5.06 (SD=0.97), 5.54 (SD=0.99), 5.139 (SD=1.30) and 6.20 (0.97) at baseline, 3 months, 6months and 12 months respectively in case group.

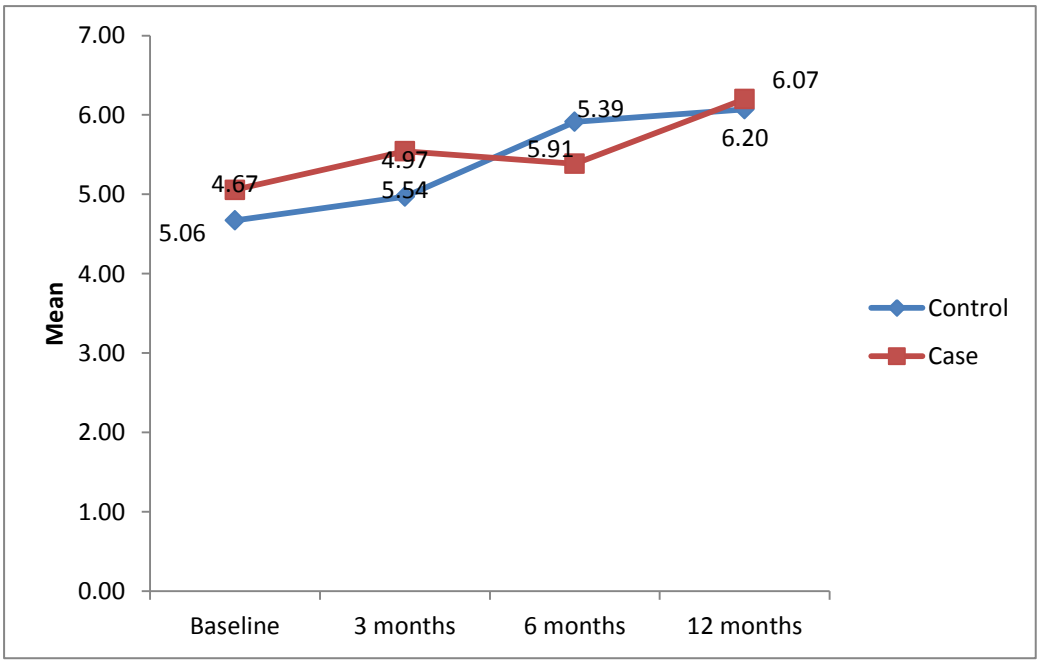


FIGURE 73: COMPARISON OF THE MEAN CREATININE OF CKD

TABLE 74a: COMPARISON OF THE DIFFERENCE OF MEAN CREATININE OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-3m	-0.30	0.96	-0.49	1.56	0.268	0.793	0.19	0.69
0-6m	-1.24	1.50	-0.33	2.11	-0.935	0.368	-0.91	0.98
0-12m	-1.40	1.28	-1.14	0.65	-0.473	0.644	-0.26	0.54
3-6m	-0.94	1.26	0.16	0.96	-1.832	0.092	-1.10	0.60
3-12m	-1.10	1.36	-0.66	1.76	-0.527	0.608	-0.44	0.84
6-12m	-0.16	0.85	-0.81	2.03	0.791	0.444	0.66	0.83

There was statistically no difference in change in the mean value of creatinine at 3, 6 and 12 months between control and case group. This was 0.30, 0.24, -0.06 at 3, 6 and 12 months for controls. This was -0.29, -0.55, -0.26 at 3, 6 and 12 months for cases.

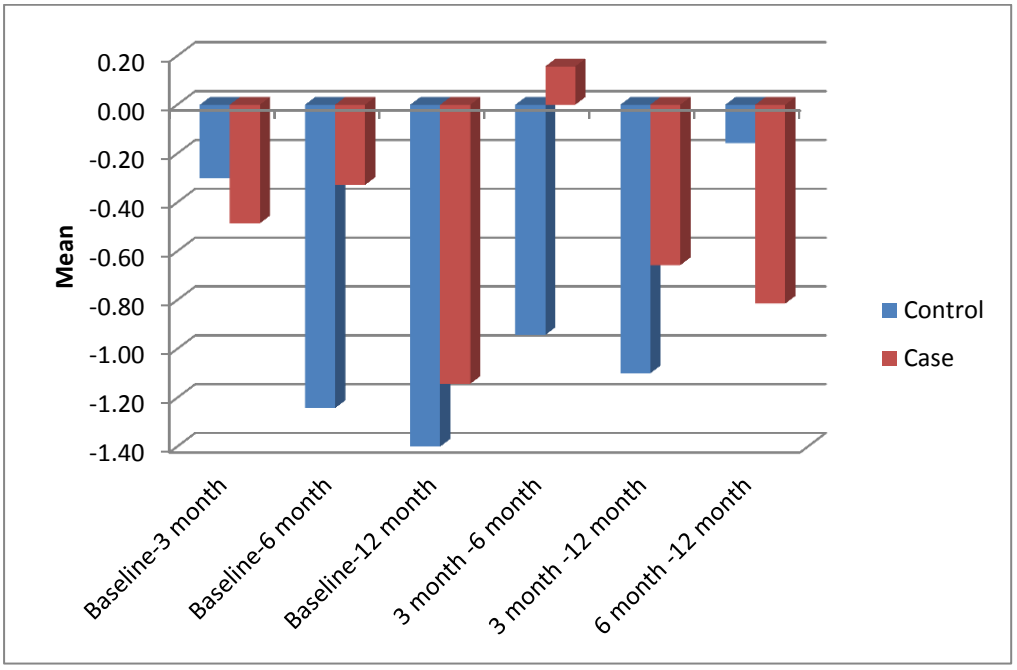


FIGURE 74a: COMPARISON OF DIFFERENCE OF MEAN CREATININE OF CKD5

TABLE 74b: COMPARISON OF MEAN eGFR FOR CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
eGFR baseline	12.00	1.83	12.14	2.27	-0.130	0.899	-0.14	1.10
eGFR at 12 months	9.57	2.51	9.43	2.15	0.114	0.911	0.14	1.25

There was no significant difference in mean e GFR between two groups at end of 12 months.

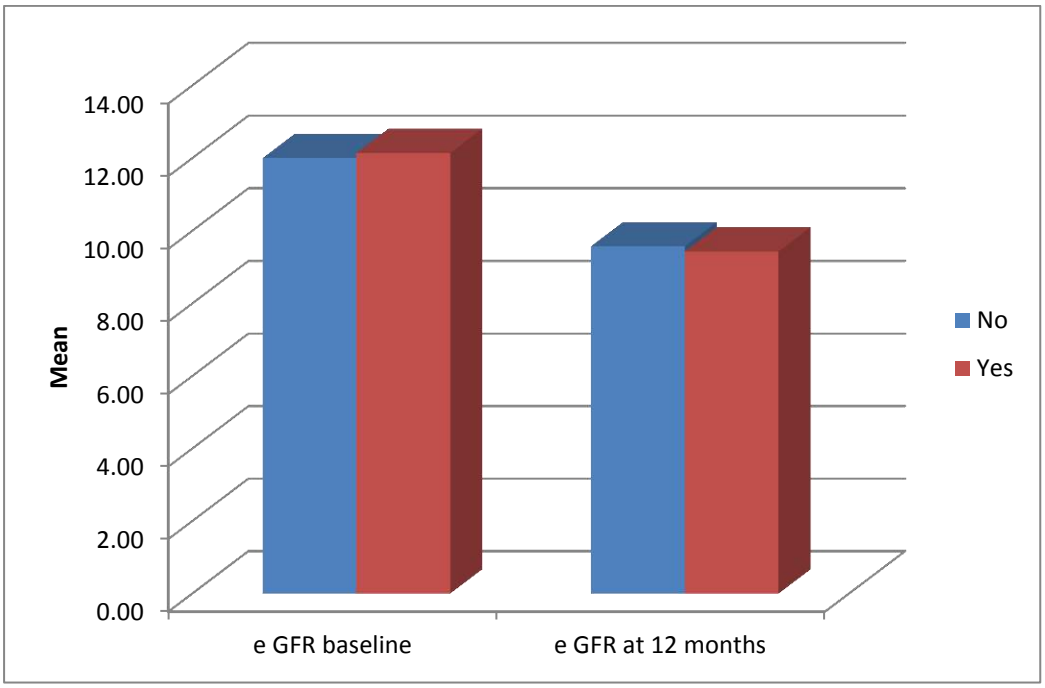


TABLE 74b: COMPARISON OF MEAN e GFR FOR CKD5

TABLE 75: COMPARISON OF THE MEAN SERUM CALCIUM VALUE OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Calcium baseline mg/dl	8.53	0.64	8.43	0.18	0.398	0.697	0.10	0.25
calcium at 3 months	8.56	0.19	8.53	0.75	0.097	0.924	0.03	0.29
calcium at 6 months	8.69	0.69	8.94	0.64	-0.722	0.484	-0.26	0.36
calcium at 12 months	8.36	0.54	8.10	0.20	1.185	0.259	0.26	0.22

There was no difference in mean calcium level at baseline, 3, 6 and 12 months between control and case group. This was 8.53, 8.56, 8.69, 8.36 at baseline, 3, 6 and 12 months for controls. This was 8.43, 8.53, 8.94, 8.10 at baseline, 3, 6 and 12 months for cases.

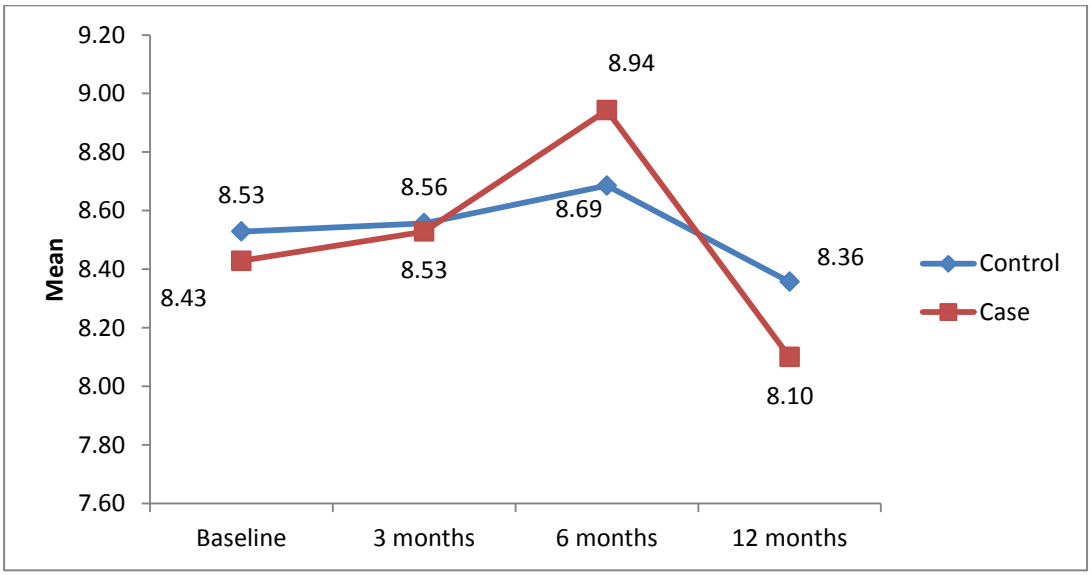


FIGURE 75: COMPARISON OF THE MEAN SERUM CALCIUM VALUE OF CKD5

TABLE 76: COMPARISON OF THE MEAN SERUM PHOSPHORUS VALUE OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean mg/dl	SD	Mean	SD			Mean	SD
Baseline	6.51	0.84	7.00	1.92	-0.614	0.551	-0.49	0.79
At 3 month	6.57	0.62	7.03	1.55	-0.725	0.482	-0.46	0.63
At 6 month	6.29	0.45	6.64	0.71	-1.129	0.281	-0.36	0.32
At 12 months	6.29	0.33	6.19	0.51	0.437	0.670	0.10	0.23

There was no difference in mean phosphorus level at baseline, 3, 6 and 12 months between control and case group. This was 6.51, 6.57, 6.29, 6.29 at baseline, 3, 6 and 12 months for controls. This was 7.00, 7.03, 6.64, 6.19 at baseline, 3, 6 and 12 months for cases.

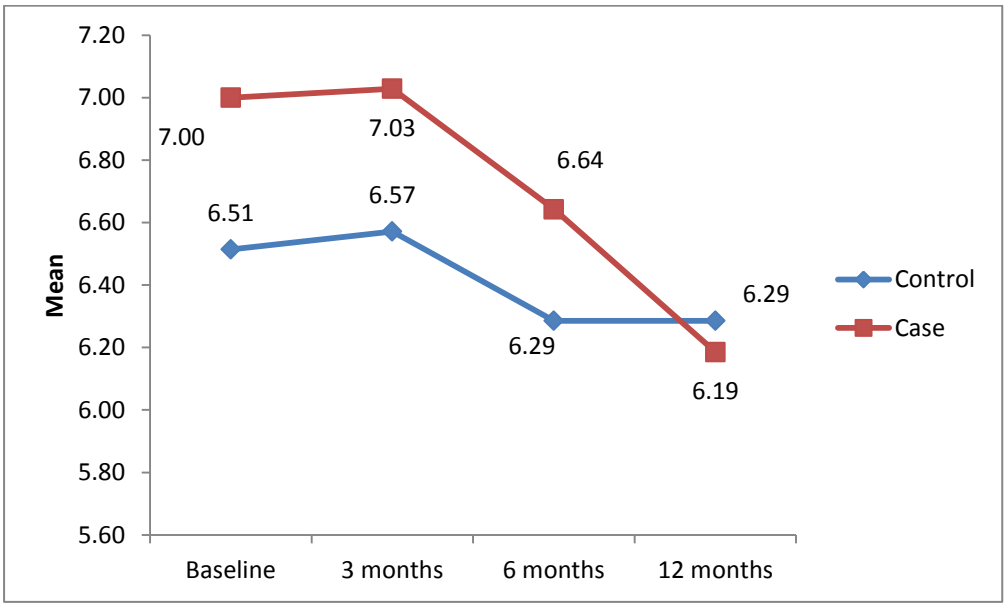


FIGURE 76: COMPARISON OF THE MEAN SERUM PHOSPHORUS VALUE OF CKD5

TABLE 77: COMPARISON OF THE MEAN SERUM ALKALINE PHOSPHATASE VALUE OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Base line U/dl	155.71	13.59	146.71	11.19	1.353	0.201	9.00	6.65
At 3 month	140.43	8.68	150.43	15.02	-1.525	0.153	-10.00	6.56
At 6 month	143.57	9.98	144.14	10.76	-0.103	0.920	-0.57	5.55
At 12 month	141.57	4.35	148.00	14.99	-1.090	0.297	-6.43	5.90

There was no difference in mean ALP level at baseline, 3, 6 and 12 months between control and case group. This was 155.71, 140.43, 143.57, 141.57 at baseline, 3, 6 and 12 months for controls. This was 146.71, 150.43, 144.14, 148.00 at baseline, 3, 6 and 12 months for cases.

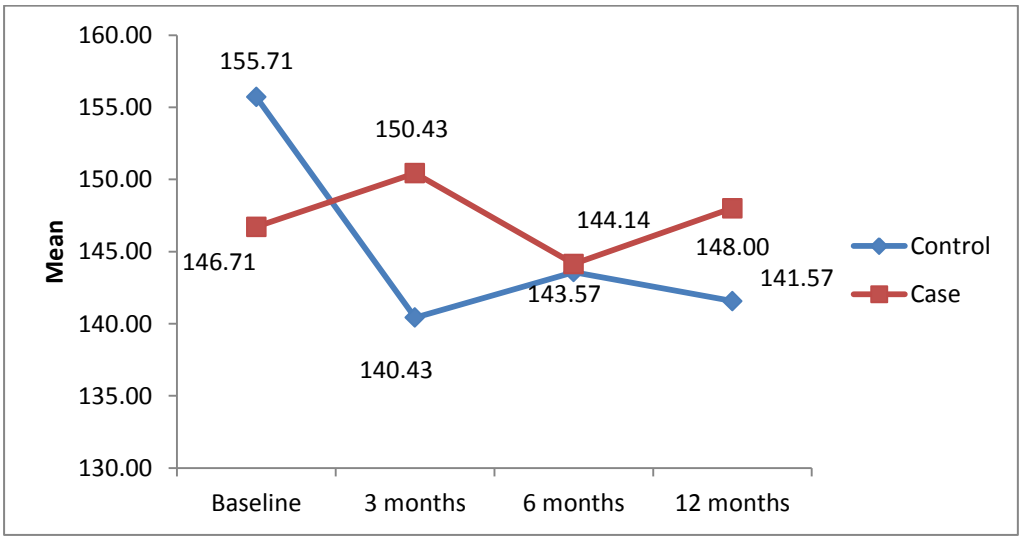


FIGURE 77: COMPARISON OF THE MEAN SERUM ALKALINE PHOSPHATASE VALUE OF CKD5

TABLE 78: COMPARISON OF THE MEAN PTH VALUES OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline pg/ml	196.57	12.70	201.43	8.75	-0.833	0.421	-4.86	5.83
At 3 months	196.57	15.06	200.71	10.70	-0.593	0.564	-4.14	6.98
At 6 months	191.14	15.33	192.43	11.03	-0.180	0.860	-1.29	7.14
At 12 months	184.86	9.81	180.43	7.74	0.938	0.367	4.43	4.72

There was no difference in mean PTH level at baseline, 3, 6 and 12 months between control and case group. PTH values were 196.57, 195.57, 191.14, 184.86, at baseline, 3, 6 and 12 months for controls. These were 201 .43, 200.71, 192.43, 180.43 at baseline, 3, 6 and 12 months for cases. But there was statistically no significance difference in mean PTH level between control and cases.

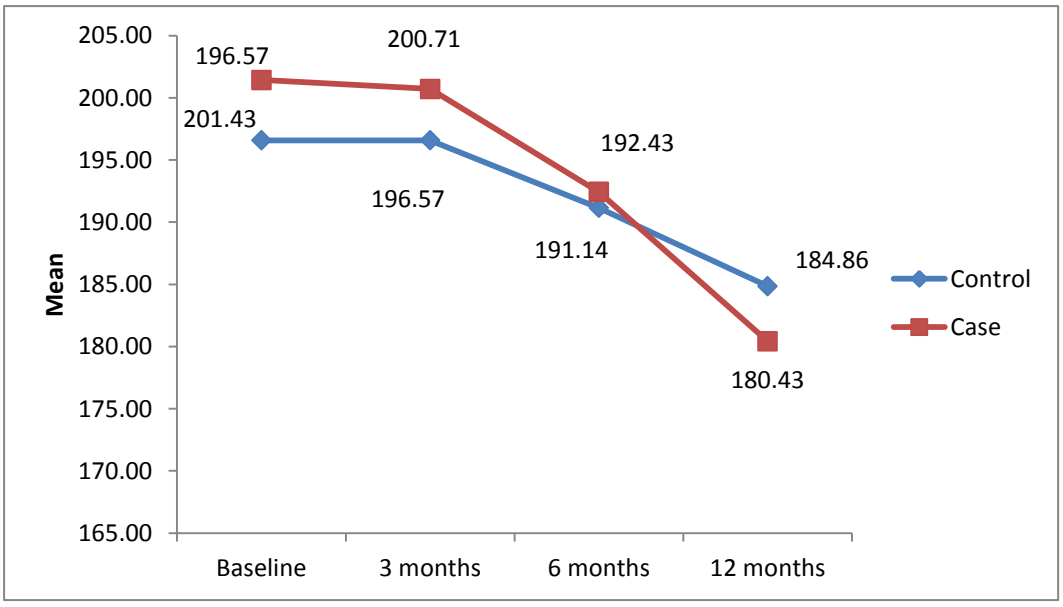


FIGURE 78: COMPARISON OF THE MEAN PTH VALUES OF CKD5

TABLE 79: COMPARISON OF DIFFERENCE IN MEAN PTH VALUE OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 3m	0.00	18.29	0.71	12.22	-0.086	0.933	-0.71	8.31
0- 6m	5.43	21.18	9.00	13.15	-0.379	0.711	-3.57	9.42
0-12m	11.71	11.40	21.00	10.77	-1.567	0.143	-9.29	5.93
3-6m	5.43	22.22	8.29	8.79	-0.316	0.757	-2.86	9.03
3-12m	11.71	16.30	20.29	8.32	-1.239	0.239	-8.57	6.92
6-12m	6.29	14.03	12.00	3.83	-1.039	0.319	-5.71	5.50

There was statistically no difference in change in the mean value of PTH at 3, 6 and 12 months between control and case group.

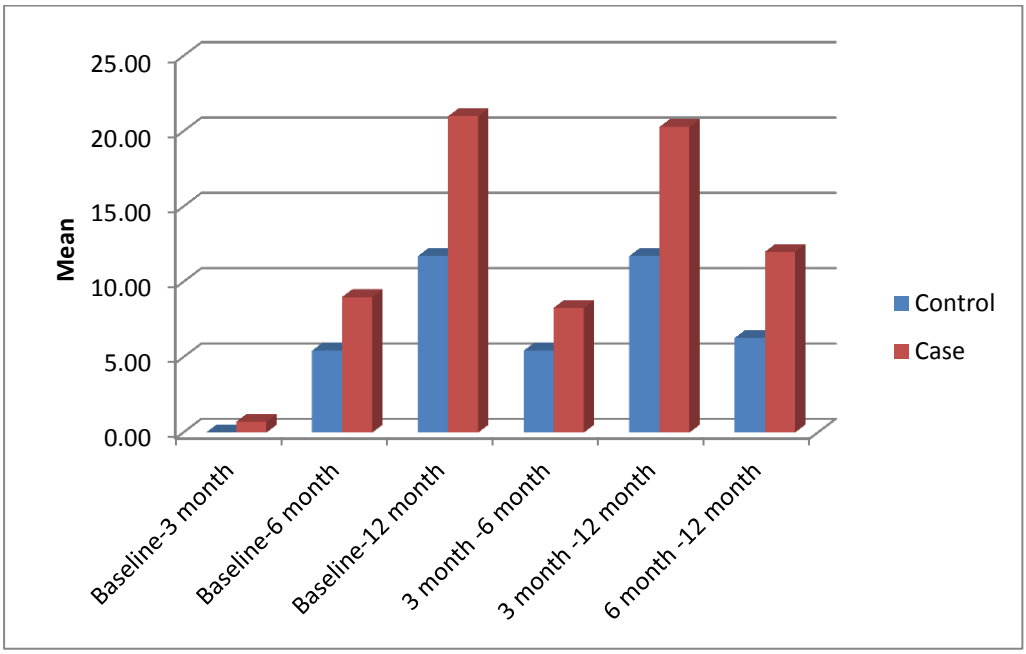


FIGURE 79: COMPARISON OF DIFFERENCE IN MEAN PTH VALUE OF CKD5

TABLE 80: COMPARISON OF THE MEAN VITAMIN D3 VALUES OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Vitamin D3 ng/ml baseline	26.86	1.68	27.43	2.44	-0.511	0.619	-0.57	1.12
Vitamin D3 at 3 months	25.43	3.36	25.71	2.14	-0.190	0.853	-0.29	1.51
Vitamin D3 at 6 months	23.43	1.51	25.14	3.18	-1.287	0.223	-1.71	1.33
Vitamin D3 at 12 months	25.57	3.26	25.14	3.39	0.241	0.813	0.43	1.78

There was no difference in mean vitamin D3 level at baseline, 3, 6 and 12 months between control and case group. This was 26.86, 25.43, 23.43, 25.57at baseline, 3, 6 and 12 months for controls. This was 27.43, 25.71, 25.14, 25.14 at baseline, 3, 6 and 12 months for cases.

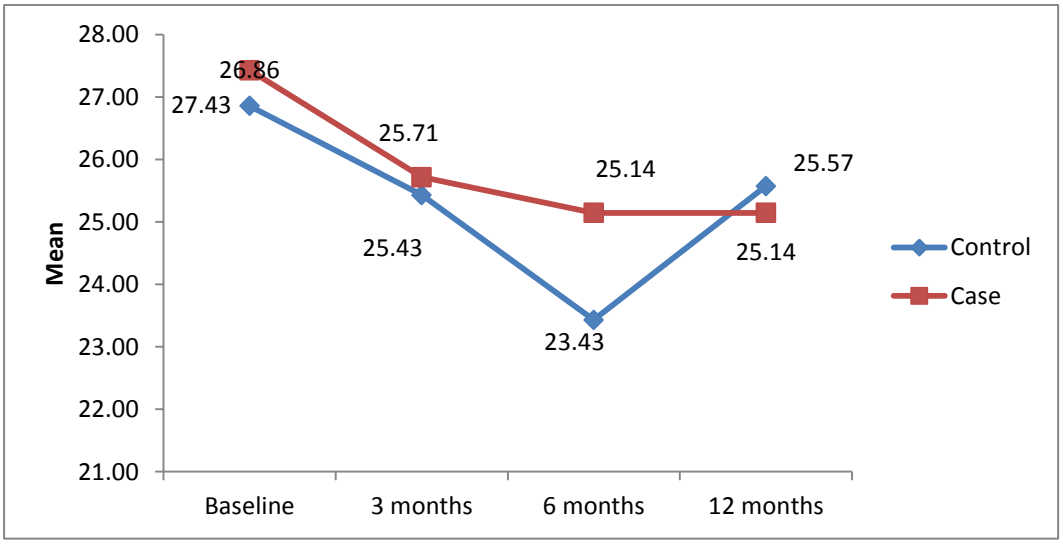


FIGURE 80: COMPARISON OF THE MEAN VITAMIN D3 VALUES OF CKD5

TABLE 81: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF LUMBAR SPINE OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6M	0.07	0.10	-0.17	0.10	4.777	0.000	0.24	0.05
0- 12M	0.17	0.20	-0.34	0.11	6.002	0.000	0.52	0.09

Mean lumbar spine T score was -1.76for case and -1.31 for control respectively at baseline. It was -1.59 and -0.39 for case and control respectively at 6 months. It was -1.41 and -1.49 or case and control respectively at 12 months. There was improvement in mean T score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of T score was statistically significant between two groups at 6and 12 month.

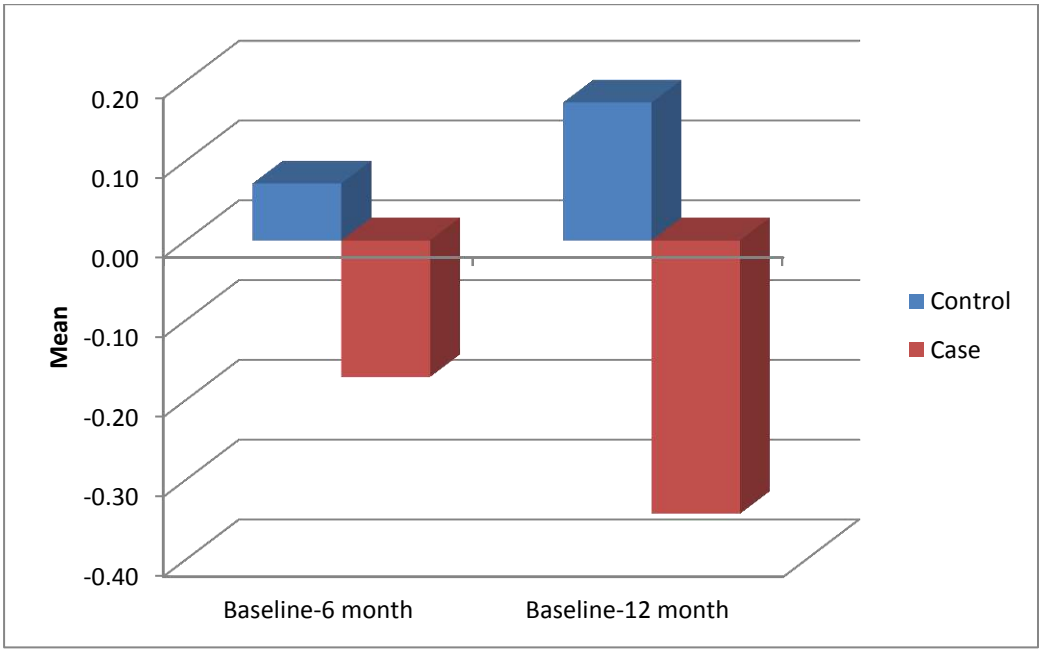


FIGURE 81: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF LUMBAR SPINE OF CKD5

TABLE 82: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF LUMBAR SPINE OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6M	0.04	0.08	-0.14	0.05	5.082	0.000	0.18	0.04
0-12M	0.09	0.19	-0.28	0.11	4.556	0.001	0.37	0.08

Mean lumbar spine Z score was -1.27 for case and -0.41 for control respectively at baseline. It was -1.13 and -0.46 for case and control respectively at 6 months. It was -0.99 and -0.50for case and control respectively at 12 months.

There was improvement in mean Z score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean Z score was statistically significant between two groups at 6 and 12 month.

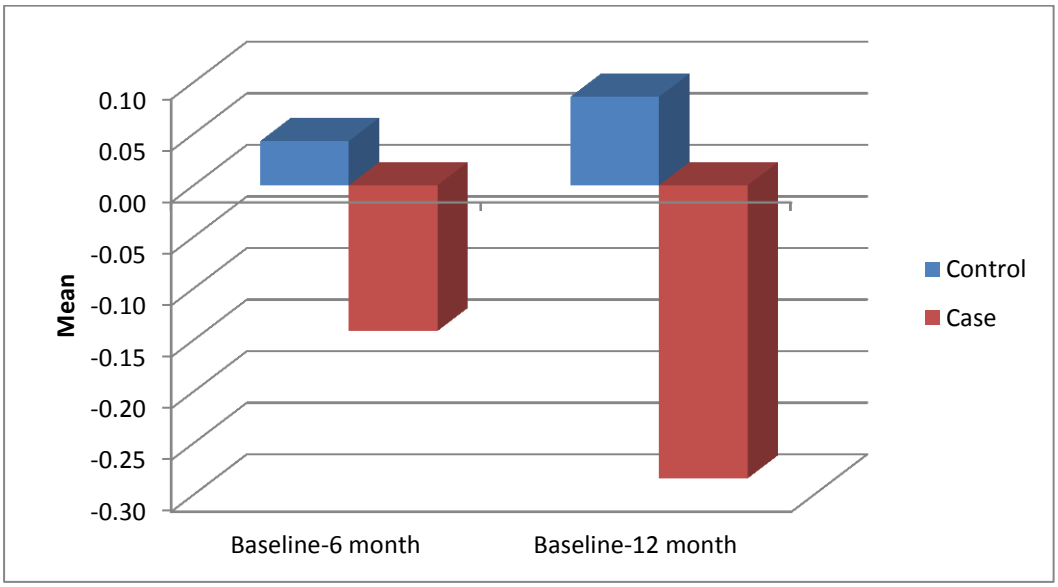


FIGURE 82: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF LUMBAR SPINE OF CKD5

TABLE 83: COMPARISON OF MEAN BMD AT LEVEL OF LUMBAR SPINE OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline in g/m2	1.16	0.33	1.02	0.16	0.951	0.361	0.13	0.14
At 6 month	1.14	0.31	1.10	0.20	0.284	0.781	0.04	0.14
At 12 month	1.08	0.31	1.26	0.22	-1.265	0.230	-0.18	0.14
DIFFERENCE 0-6M	0.02	0.04	-0.07	0.06	3.233	0.007	0.09	0.03
DIFFERENCE 0- 12M	0.07	0.09	-0.24	0.08	6.700	0.000	0.31	0.05

Mean lumbar spine BMD was 1.02 for case and 1.16 for control respectively at baseline. It was 1.10 and 1.14 for case and control respectively at 6 months. It was 1.26 and 1.08 for case and control respectively at 12 month.

There was improvement in mean BMD at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in change in mean BMD was statistically significant between two groups at 6 and 12 month.

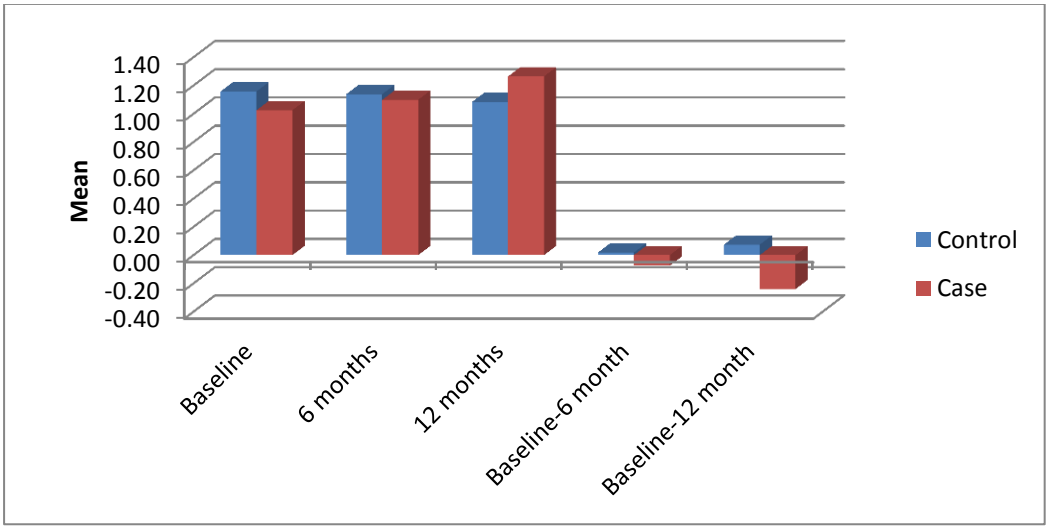


FIGURE 83: COMPARISON OF MEAN BMD AT LEVEL OF LUMBAR SPINE OF CKD5

TABLE 84: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF FEMUR NECK OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6M	0.05	0.16	-0.21	0.11	3.675	0.003	0.27	0.07
0-12M	0.10	0.28	-0.41	0.11	4.500	0.001	0.51	0.11

Mean femur neck T score was -2.20 for case and -1.80 for control respectively at baseline. It was -1.99 and -1.85for case and control respectively at 6 months. It was -1.79 and -1.90 for case and control respectively at 12 month.

There was improvement in mean T score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean T score was statistically significant between two groups at 6 and 12 month.

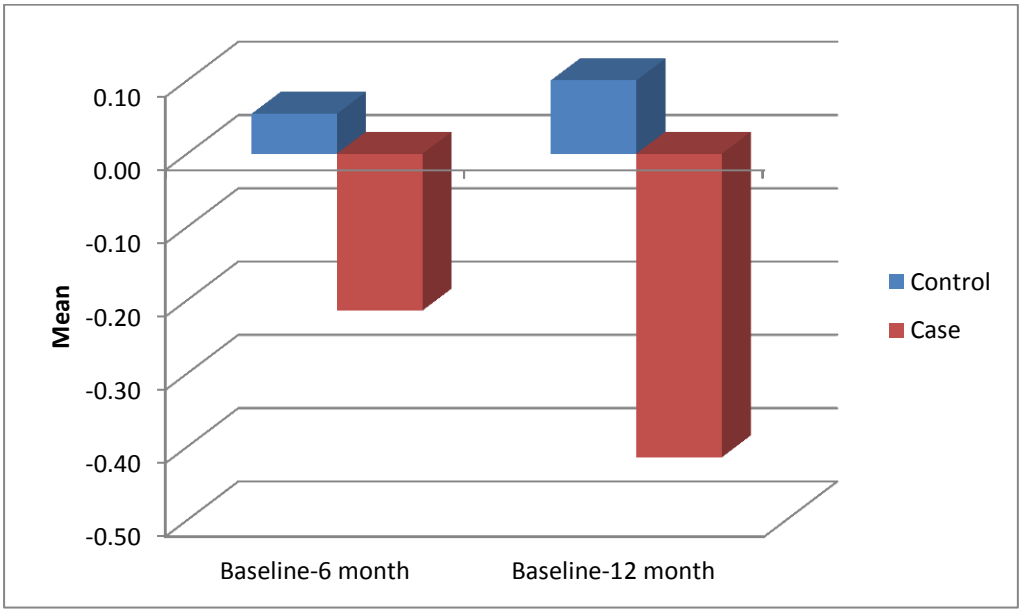


FIGURE 84: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF FEMUR NECK OF CKD5

TABLE 85: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF FEMUR NECK OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6M	0.03	0.11	-0.14	0.10	3.065	0.010	0.17	0.06
0- 12M	0.13	0.21	-0.33	0.11	5.018	0.000	0.46	0.09

Mean femur neck Z score was -1.20 for case and -0.40 for control respectively at baseline. It was -0.06 and -0.43 for case and control respectively at 6 months. It was -0.86 and -0.53 for case and control respectively at 12 months.

There was improvement in mean Z score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean Z score was statistically significant between two groups at 6 and 12 month.

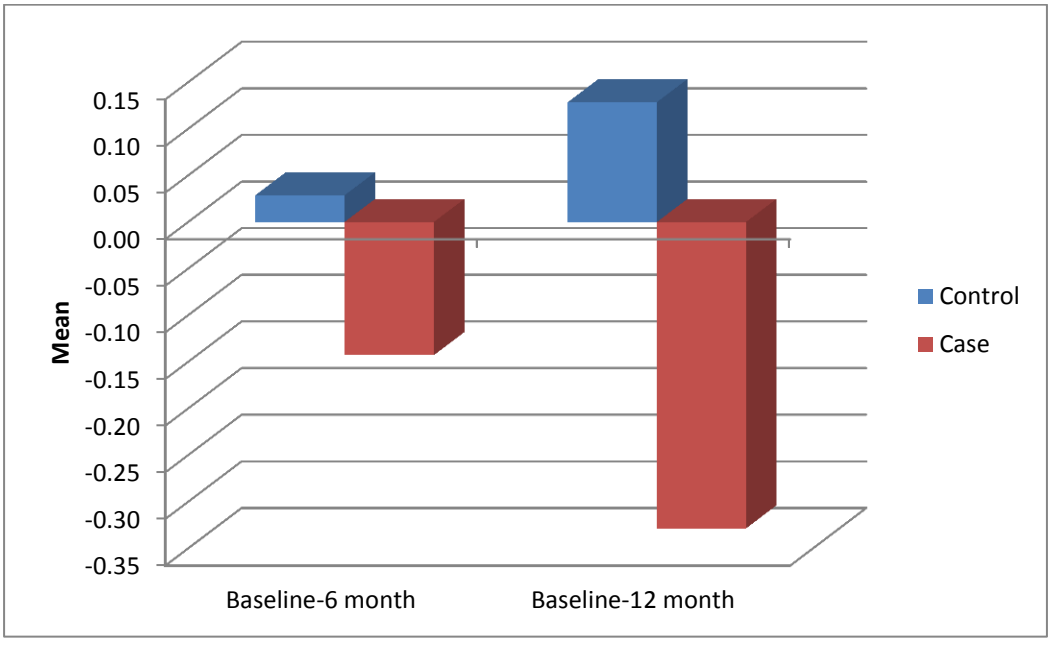


FIGURE 85: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF FEMUR NECK OF CKD5

TABLE 86: COMPARISON OF MEAN BMD AT LEVEL OF FEMUR NECK OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline in g/cm2	0.81	0.17	0.81	0.20	0.040	0.969	0.00	0.10
At 6 month	0.78	0.15	0.94	0.33	-1.179	0.261	-0.16	0.14
At 12 month	0.77	0.17	1.04	0.31	-2.043	0.064	-0.27	0.13
DIFFERENCE 0-6M	0.04	0.07	-0.13	0.17	2.361	0.036	0.17	0.07
DIFFERENCE 0-12M	0.04	0.12	-0.23	0.15	3.842	0.002	0.27	0.07

Mean femur neck BMD was 0.81 for case and 0.81 for control respectively at baseline. It was 0.94 and 0.78 for case and control respectively at 6 months. It was 1.04 and 0.77for case and control respectively at 12 month.

There was improvement in mean BMD at level of femur neck at 6 and 12 months in change in mean BMD was statistically significant between two groups at 6 and 12 month.

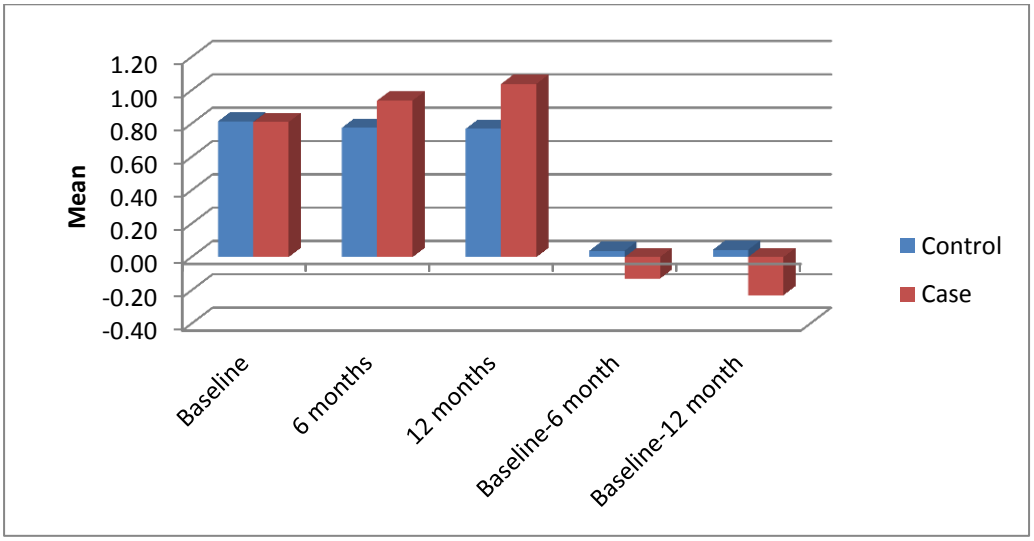


FIGURE 86: COMPARISON OF MEAN BMD AT LEVEL OF FEMUR NECK OF CKD5

TABLE 87: COMPARISON OFTHE DIFFERENCE OF MEAN T SCORE OF TOTAL HIP OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6M	0.07	0.13	-0.11	0.12	2.815	0.016	0.19	0.07
0-12M	0.10	0.27	-0.30	0.13	3.514	0.004	0.40	0.11

Mean total hip T score was -1.69 for case and -1.27 for control respectively at baseline. It was -1.57 and -1.34 for case and control respectively at 6 months. It was -1.39 and -1.37 for case and control respectively at 12 month.

There was improvement in mean T score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in change in mean T score was statistically significant between two groups at 6 and 12 month.

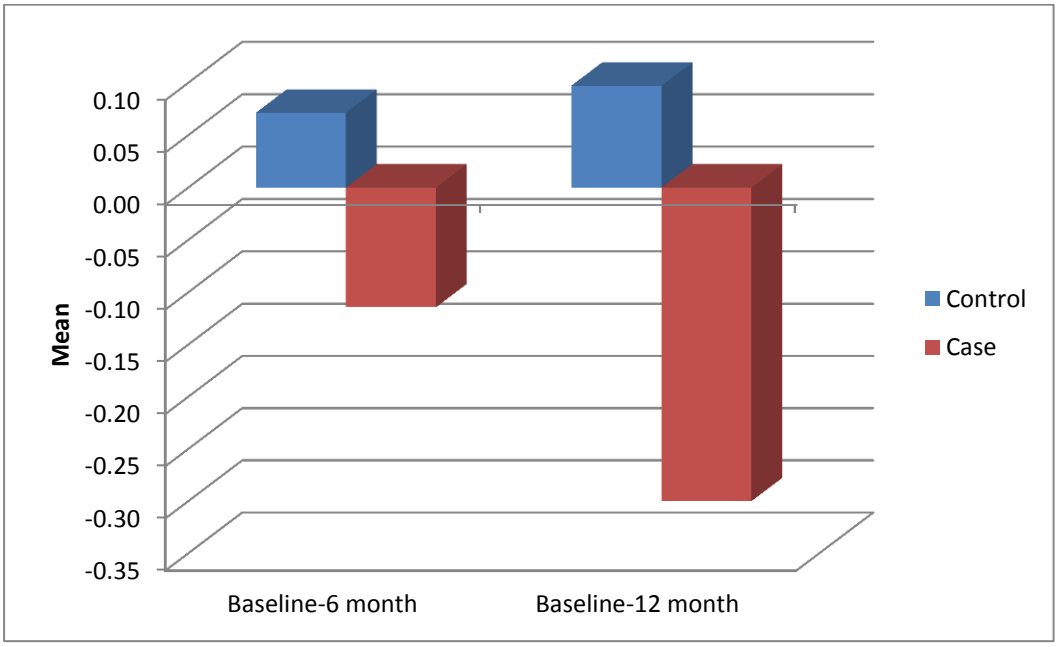


FIGURE 87: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE OF TOTAL HIP OF CKD5

TABLE 88: COMPARISON OFTHE DIFFERENCE OF MEAN Z SCORE OF TOTAL HIP OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6M	0.00	0.14	-0.11	0.09	1.804	0.096	0.11	0.06
0-12M	-0.49	1.14	-0.33	0.15	-0.362	0.723	-0.16	0.43

Mean total hip Z score was -1.04 for case and -0.80 for control respectively at baseline. It was -0.93 and -0.80 for case and control respectively at 6 months. It was -0.71 and -0.31 for case and control respectively at 12 months.

There was improvement in mean Z score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. But this difference in change in mean Z score was not statistically significant between two groups at 6 and 12 month.

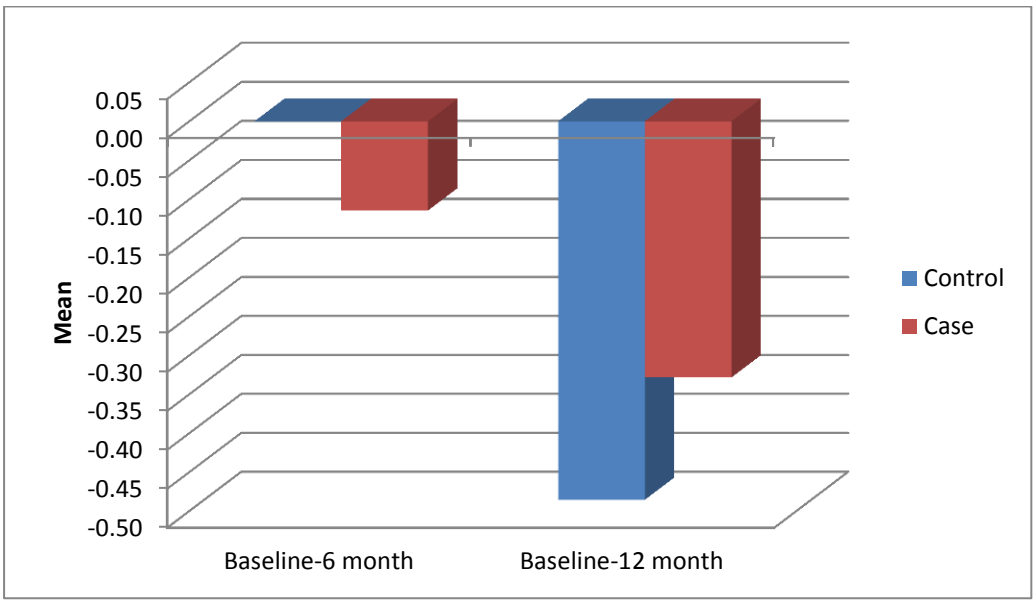


FIGURE 88: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE OF TOTAL HIP OF CKD5

TABLE 89: COMPARISON OF MEAN BMD OF TOTAL HIP OF CKD5

CKD 5 stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline in g/m2	0.89	0.20	0.81	0.22	0.738	0.475	0.08	0.11
At 6 Month	0.86	0.21	0.94	0.32	-0.506	0.622	-0.07	0.14
At 12 Month	0.84	0.21	1.03	0.32	-1.295	0.220	-0.19	0.14
DIFFERENCE 0-6M	0.03	0.05	-0.13	0.14	2.798	0.016	0.16	0.06
DIFFERENCE 0-12M	0.05	0.12	-0.22	0.15	3.853	0.002	0.27	0.07

Mean total hip BMD was 0.81 for case and 0.89 for control respectively at baseline. It was 0.94 and 0.86 for case and control respectively at 6 months. It was 1.03 and 0.84 for case and control respectively at 12 month.

There was improvement in mean BMD at level of total hip at 6 and 12 month in patients, who received oral alendronate compared to controls. This difference in change in mean BMD was statistically significant between two groups at 6 and 12 month.

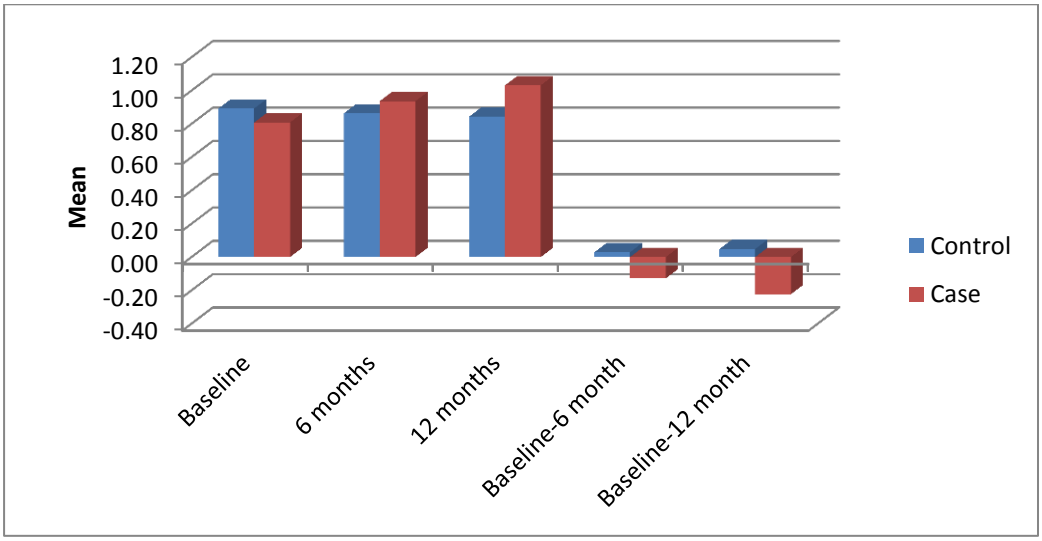


FIGURE 89: COMPARISON OF MEAN BMD OF TOTAL HIP OF CKD5

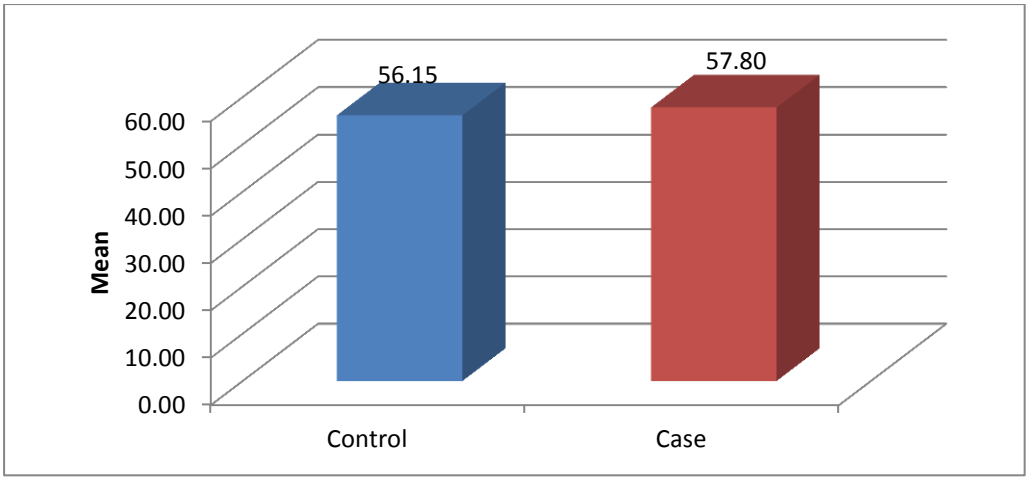
TABLE 90: COMPARISON OF BASELINE DEMOGRAPHIC FEATURES OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Age	56.15	11.23	57.80	7.68	-0.542	0.591	-1.65	3.04
Duration of dialysis at time of enrollment in months	11.95	14.72	21.55	22.21	-1.611	0.115	-9.60	5.96
frequency per week	2.00	0.32	2.10	0.45	-0.809	0.423	-0.10	0.12
Weight in Kg	63.77	10.99	65.68	14.04	-0.478	0.636	-1.90	3.99
Height in cm	165.80	4.63	167.20	3.96	-1.028	0.310	-1.40	1.36
SBP	130.00	6.99	131.70	11.07	-0.581	0.565	-1.70	2.93
DBP	82.50	4.63	82.30	5.20	0.128	0.898	0.20	1.56

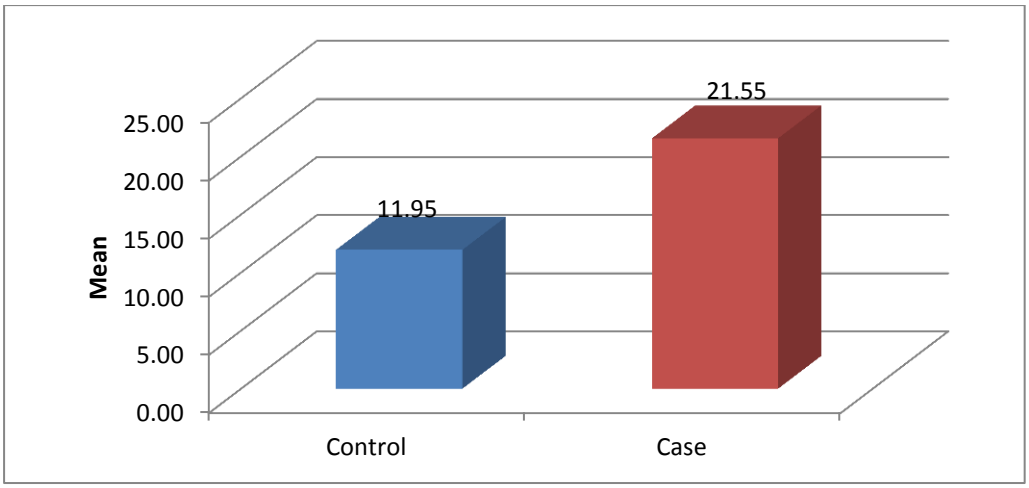
		Alendronate given by oral route				Total
		Control		Case		
Access for HD	AV fistula	17	42.5%	18	45.0%	35
	permanent dialysis catheter	0	0.0%	2	5.0%	2
	temporary right jugular catheter	3	7.5%	0	0.0%	3

						Total
		Control		Case		
Frequency per week	1	1	2.5%	1	2.5%	2
	2	18	45.0%	16	40.0%	34
	3	1	2.5%	3	7.5%	4

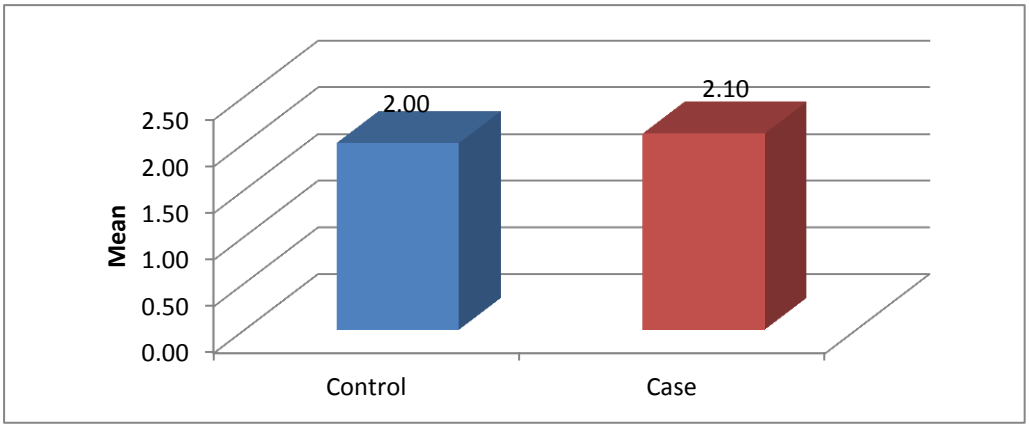
Mean age of control and case group was 56.15 (SD=11.23) and 57.80 (SD=7.68) respectively. There was no statistically difference between two groups.



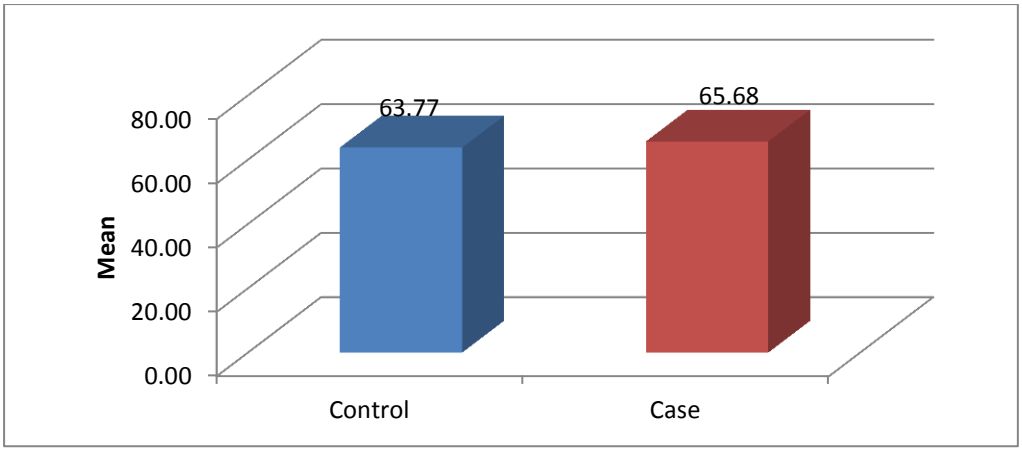
Mean duration of dialysis was 11.95 (SD=14.72) and 21.54 (SD=22.21) months in control and case group respectively.



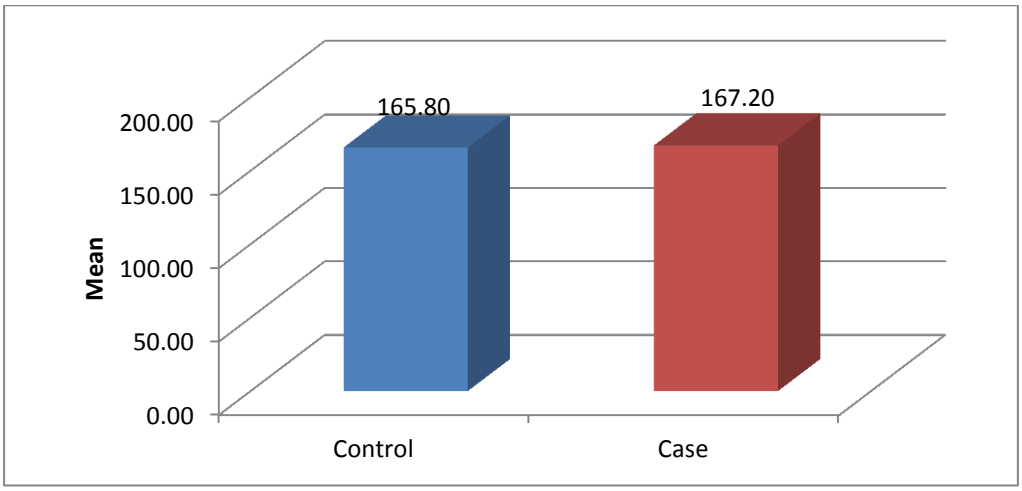
Mean frequency of dialysis was 2 (SD=0.32) and 2.1(SD=0.45) in control and case group respectively.



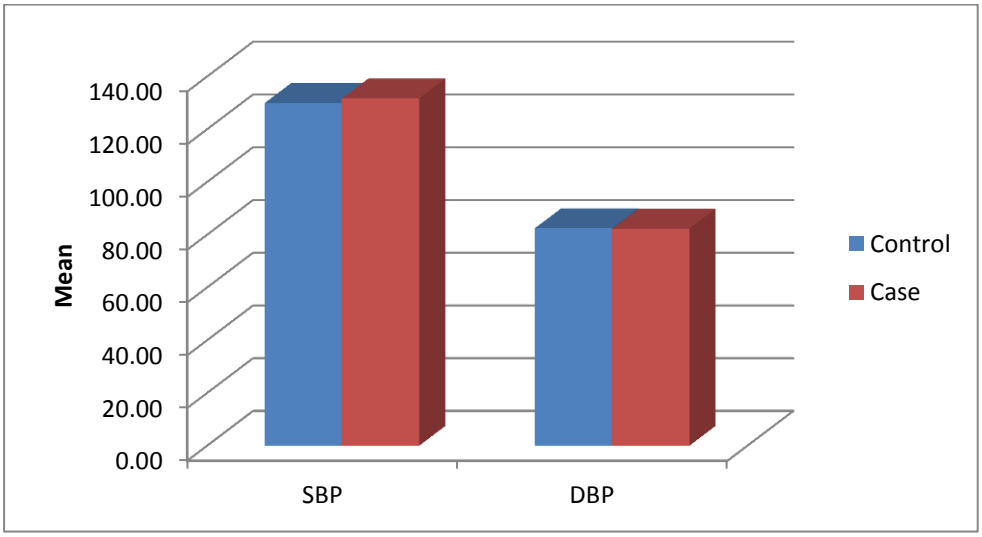
Mean weight of control and case group was 63.77 (SD=10.99) and 65.68 (SD=14.04) respectively. There was no statistically difference between two groups.

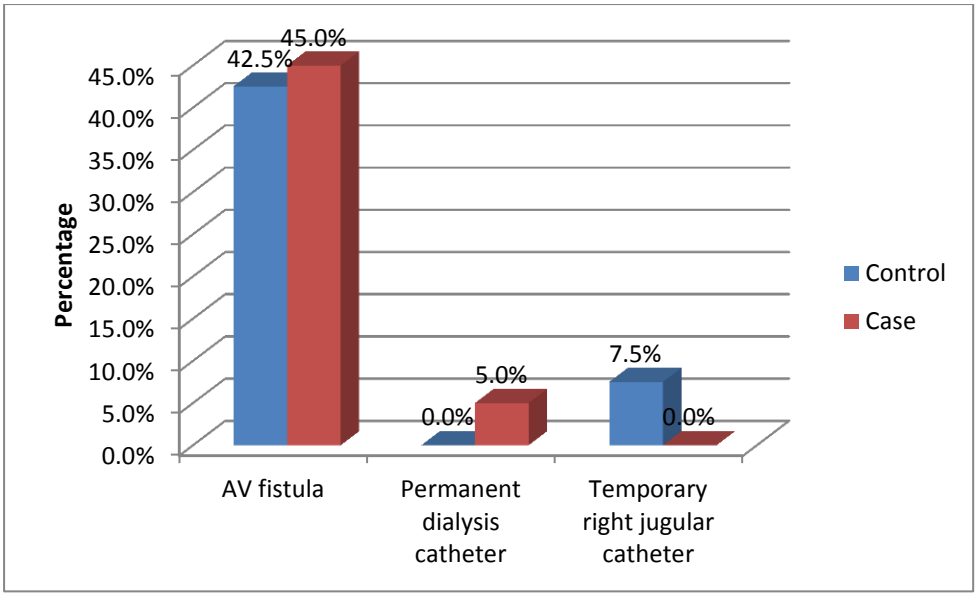


Mean height of control and case group was 165.80 (SD=4.63) and 167.20 (SD=3.96) respectively. There was no statistically difference between two groups.



Mean SBP for control and case group was130.00 (SD= 6.99) and 131.70 (SD= 11.07) respectively. Mean DBP for control and case group was 82.50 (SD= 4.63) and 82.30 (SD= 5.20) respectively.





AV fistula was most common HD access in both case and control group. Most patients were on twice a week hemodialysis in both groups.

FIGURE 90: COMPARISON OF BASELINE DEMOGRAPHIC FEATURES OF CKD5D

TABLE 91: COMPARISON OF BASELINE COMPLETE BLOOD COUNTS OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Hemoglobin baseline g/dl	9.39	0.49	9.40	0.69	-0.053	0.958	-0.01	0.19
TLC baseline per ul	8.33	1.38	8.80	1.42	-1.064	0.294	-0.47	0.44
Platelets at baseline lakh	1.48	0.22	1.60	0.42	-1.123	0.269	-0.12	0.11

Baseline mean hemoglobin was 9.39 (SD= 0.49) and 9.40 (SD= 0.69) for control and case group respectively. Baseline TLC was 8.33 (SD=1.38) and 8.80 (SD=1.42) for control and case group respectively. Baseline platelet count was 1.48 (SD=0.252) and 1.60 (SD=0.42) for control and case group respectively.

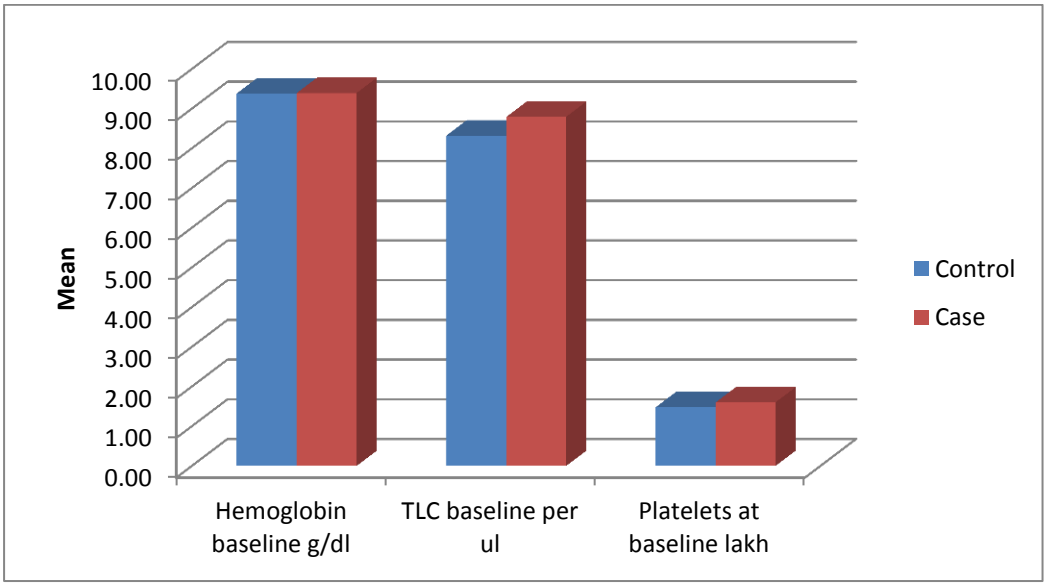


FIGURE 91: COMPARISON OF BASELINE COMPLETE BLOOD COUNTS OF CKD5D

TABLE 92: COMPARISON OF THE MEAN UREA AND CREATININEAT BASELINEOF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Urea at baseline mg/dl	131.35	12.33	133.85	19.64	-0.482	0.633	-2.50	5.19
Creatinine baseline mg/dl	4.22	0.96	4.57	0.85	-1.226	0.228	-0.35	0.29

Baseline mean urea was 131.35SD= 12.33) and 133.585 (SD= 19.64) for control and case group respectively. Baseline mean creatinine was 4.22(SD= 0.96) and 4.57(SD= 0.85) for control and case group respectively.

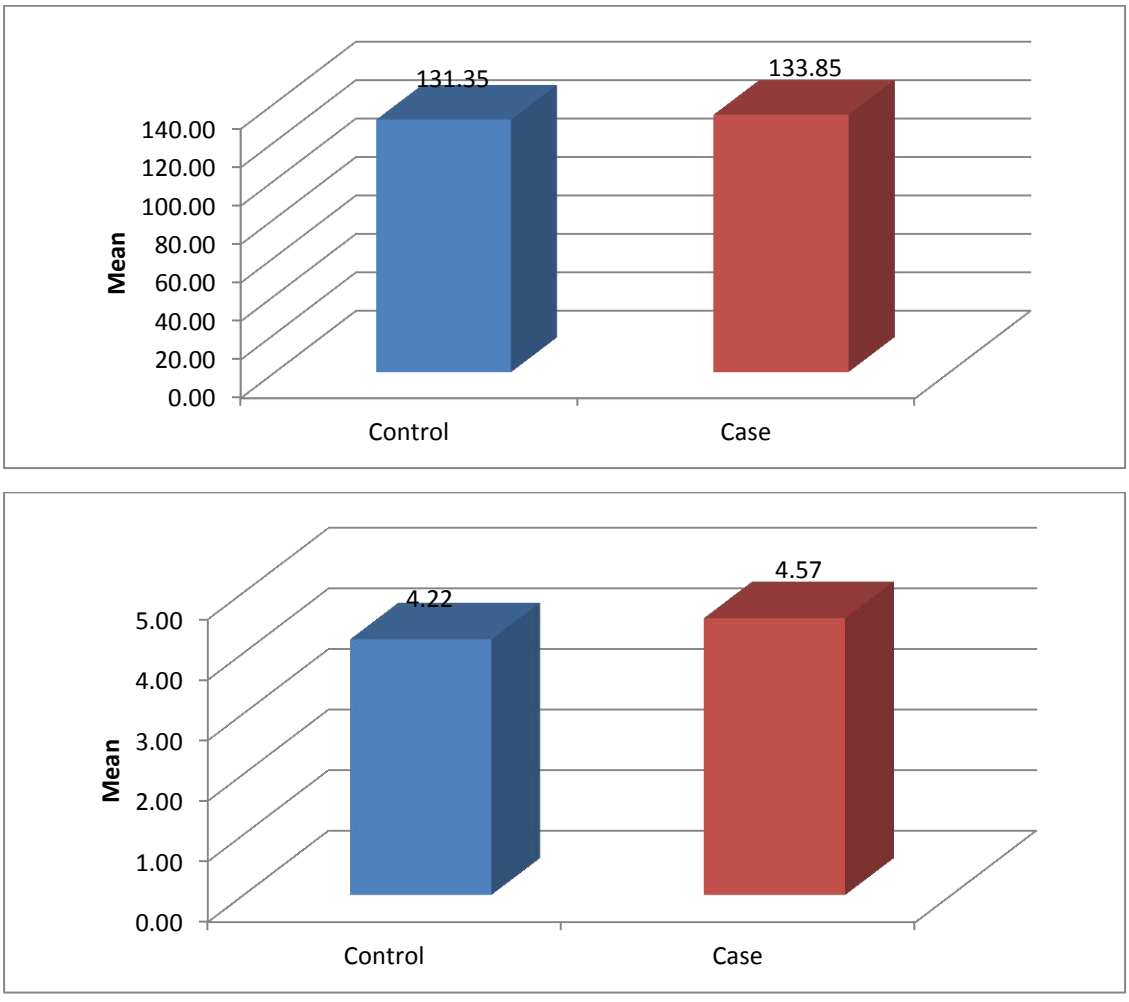
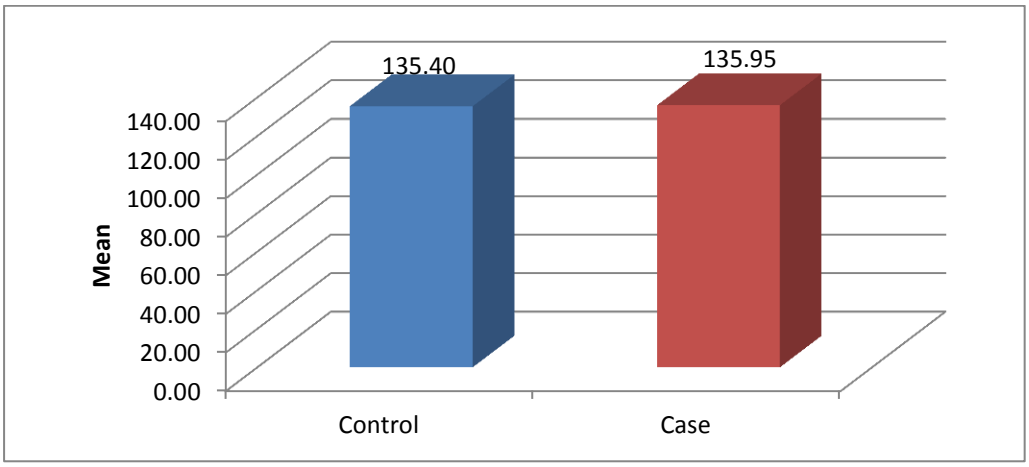


FIGURE 92: COMPARISON OF THE MEAN UREA AND CREATININE AT BASELINE OF CKD5D

TABLE 93: COMPARISON OF THE MEAN SODIUM AND POTASSIUM AT BASELINEOF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Sodium baseline meq/l	135.40	5.05	135.95	8.92	-0.240	0.812	-0.55	2.29
Potassium at baseline meq/l	4.52	1.14	4.62	0.98	-0.283	0.779	-0.10	0.34

Baseline mean sodium was 135.40(SD= 5.05) and135.95 (SD= 8.92) for control and case group respectively. Baseline mean ptassium was 4.52 (SD= 1.14) and 4.62 (SD= 0.98) for control and case group respectively.



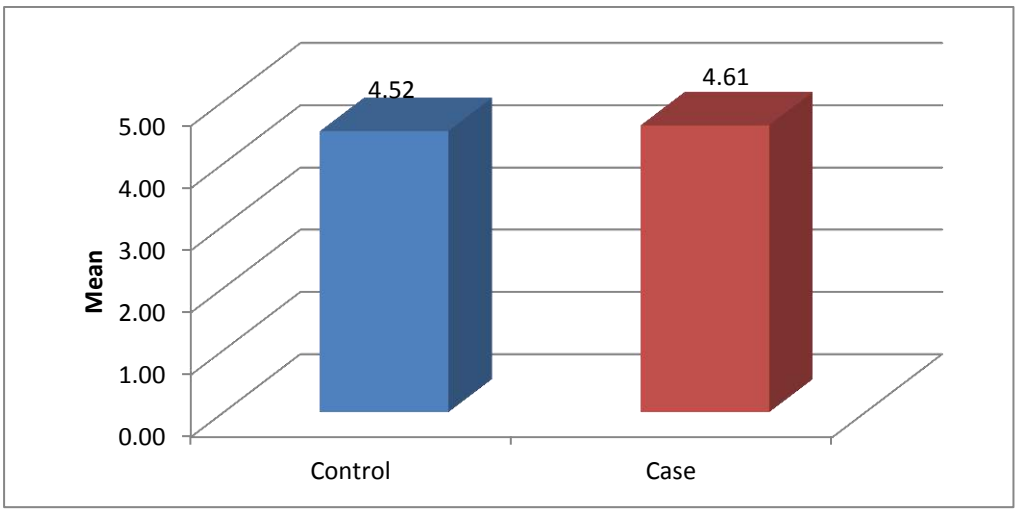


FIGURE 93: COMPARISON OF THE MEAN SODIUM AND POTASSIUM AT BASELINE OF CKD5D

TABLE 94: COMPARISON OF THE MEAN CREATININE OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline mg/dl	4.22	0.96	4.57	0.85	-1.226	0.228	-0.35	0.29
At 3 month	4.81	1.02	4.43	1.14	1.095	0.280	0.38	0.34
At 6 month	4.51	0.94	4.72	1.16	-0.629	0.533	-0.21	0.33
At 12 month	4.57	1.04	4.98	1.17	-1.173	0.248	-0.41	0.35

Mean creatinine values were 4.22 (SD=0.96), 4.81 (SD=1.02), 4.51 (SD=0.94) and 4.57 (1.04) at baseline, 3 months, 6months and 12 months respectively in control group. Mean creatinine values were 4.57(SD=0.85), 4.43(SD=1.14), 4.72(SD=1.16) and 4.98 (1.17) at baseline, 3 months, 6months and 12 months respectively in case group.

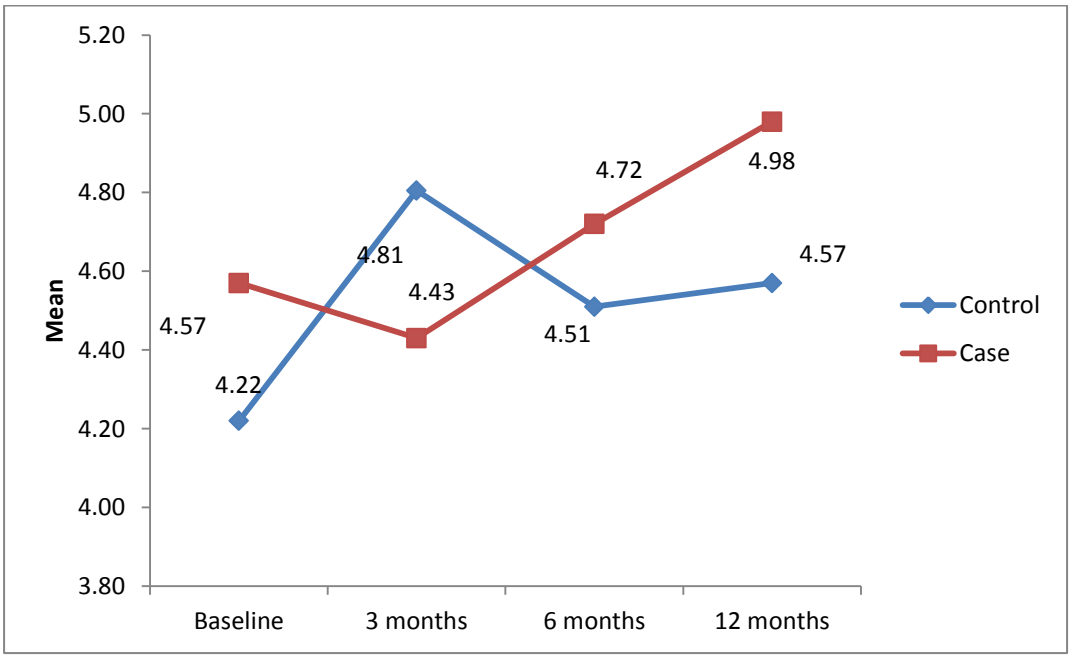


FIGURE 94: COMPARISON OF THE MEAN CREATININE OF CKD5D

TABLE 95: COMPARISON OF THE DIFFERENCE OF MEAN CREATININE OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-3m	-0.59	1.28	0.14	1.28	-1.792	0.081	-0.73	0.40
0-6m	-0.29	1.23	-0.15	1.49	-0.324	0.747	-0.14	0.43
0-12m	-0.35	1.41	-0.41	1.39	0.135	0.893	0.06	0.44
3-6m	0.30	1.00	-0.29	1.45	1.483	0.146	0.59	0.39
3-12m	0.24	1.75	-0.55	1.81	1.398	0.170	0.79	0.56
6-12m	-0.06	1.51	-0.26	1.15	0.471	0.640	0.20	0.42

There was statistically no difference in change in the mean value of creatinine at 3, 6 and 12 months between control and case group. This was 0.30, 0.24, -0.06 at 3, 6 and 12 months for controls. This was -0.29, -0.55, -0.26 at 3, 6 and 12 months for cases.

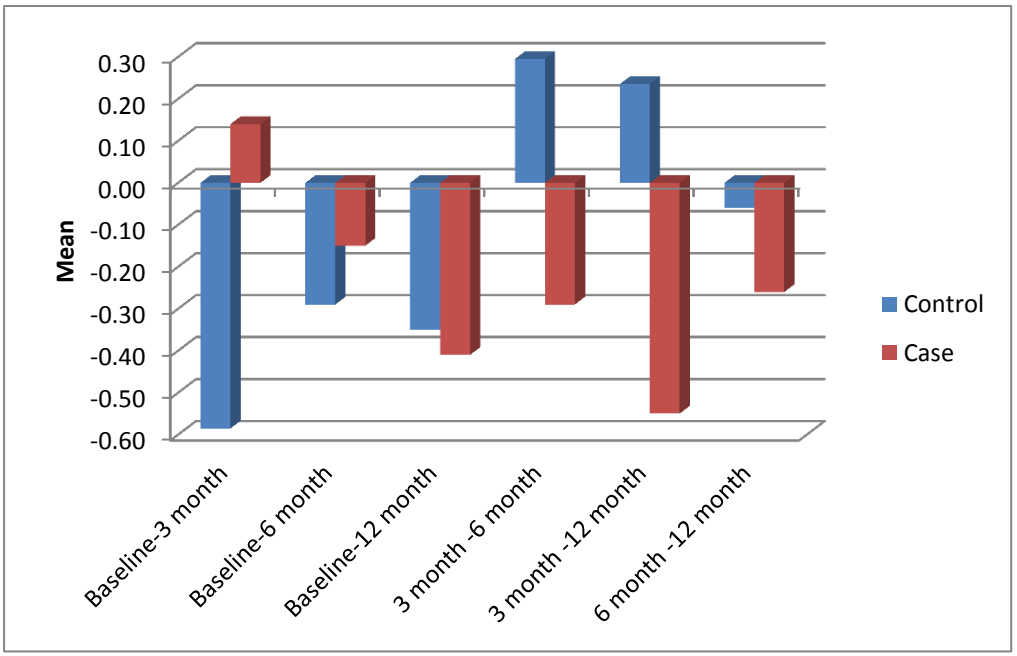


FIGURE 95: COMPARISON OF THE DIFFERENCE OF MEAN CREATININE OF CKD5D

TABLE 96: COMPARISON OF THE MEAN SERUM CALCIUM VALUE OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Calcium baseline mg/dl	8.64	0.58	8.66	0.49	-0.117	0.907	-0.02	0.17
Calcium at 3 months	8.46	0.63	8.57	0.47	-0.630	0.533	-0.11	0.17
Calcium at 6 months	8.46	0.42	8.43	0.62	0.180	0.858	0.03	0.17
Calcium at 12 months	8.55	0.78	8.49	0.57	0.277	0.783	0.06	0.22

There was no difference in mean calcium level at baseline, 3, 6 and 12 months between control and case group. This was 8.64, 8.46, 8.46, 8.55 at baseline, 3, 6 and 12 months for controls. This was 8.66, 8.57, 8.43, 8.49 at baseline, 3, 6 and 12 months for cases.

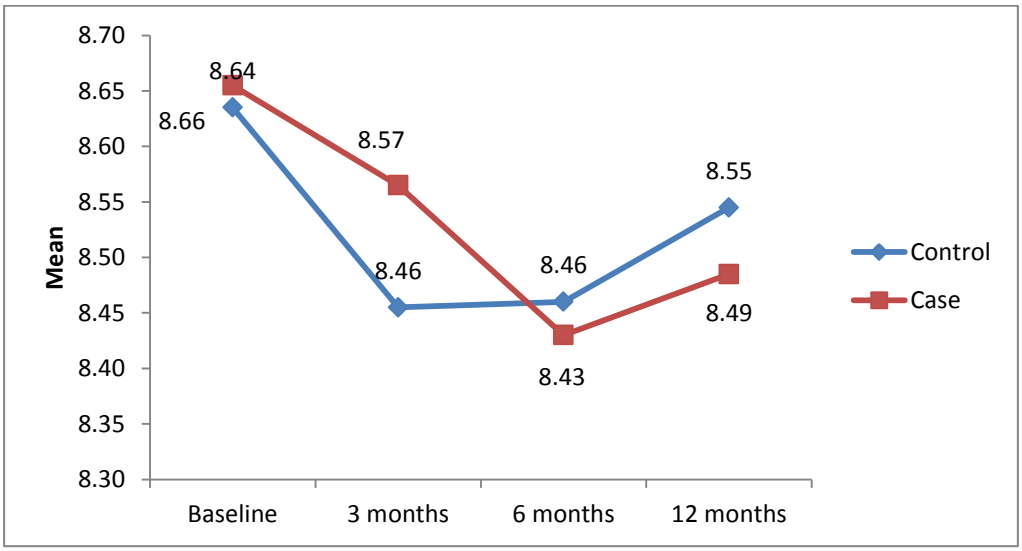


FIGURE 96: COMPARISON OF THE MEAN SERUM CALCIUM VALUE OF CKD5D

TABLE 97: COMPARISON OF THE MEAN SERUM PHOSPHORUS VALUE OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Phosphorus mg/dl baseline	6.90	1.71	6.33	0.73	1.359	0.182	0.56	0.42
Phosphorus at 3 month	6.35	0.79	6.46	0.57	-0.504	0.617	-0.11	0.22
Phosphorus at 6 month	6.92	1.36	6.58	0.81	0.962	0.342	0.34	0.35
Phosphorus at 12 month	7.21	1.53	6.70	0.74	1.328	0.192	0.51	0.38

There was no difference in mean phosphorus level at baseline, 3, 6 and 12 months between control and case group. This was 6.90, 6.35, 6.92, 7.21 at baseline, 3, 6 and 12 months for controls. This was 6.33, 6.46, 6.58, 6.70 at baseline, 3, 6 and 12 months for cases.

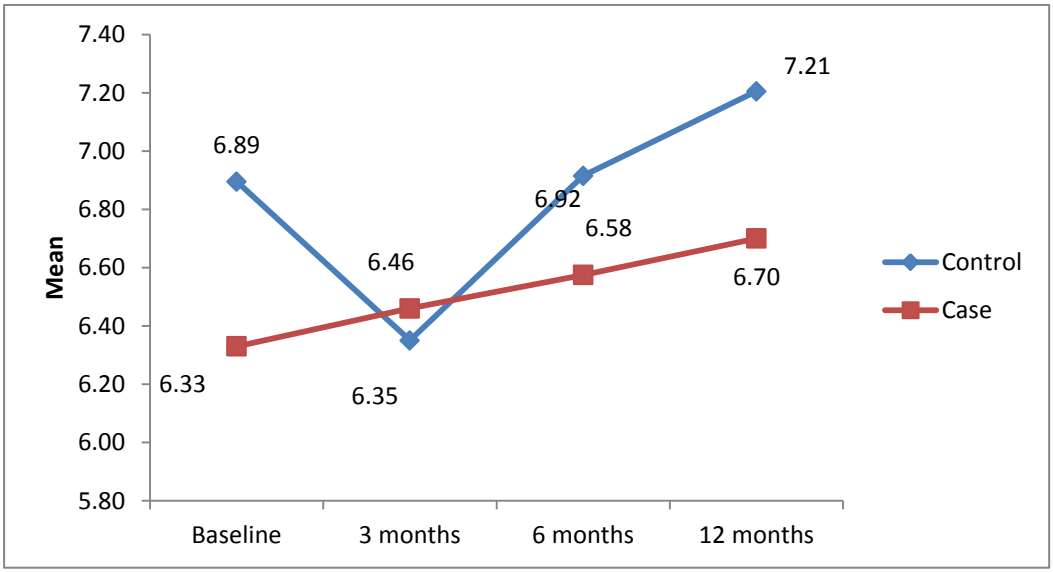


FIGURE 97: COMPARISON OF THE MEAN SERUM PHOSPHORUS VALUE OF CKD5D

TABLE 98: COMPARISON OF THE MEAN SERUM ALKALINE PHOSPHATASE VALUE OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
ALP base line	149.10	12.14	145.70	12.94	0.857	0.397	3.40	3.97
ALP at 3 months	146.70	12.17	151.75	16.66	-1.095	0.281	-5.05	4.61
ALP at 6 months	148.20	11.93	146.25	13.73	0.479	0.634	1.95	4.07
ALP at 12 months	146.80	10.01	136.85	14.88	2.481	0.018	9.95	4.01

There was no difference in mean ALP level at baseline, 3, and 6 months between control and case group. But difference was significant at 12 months. The mean ALP was 149.10, 146.70, 148.20, 146.80 at baseline, 3, 6 and 12 months for controls. This was 145.70, 151.75, 146.25, 136.85 at baseline, 3, 6 and 12 months for cases.

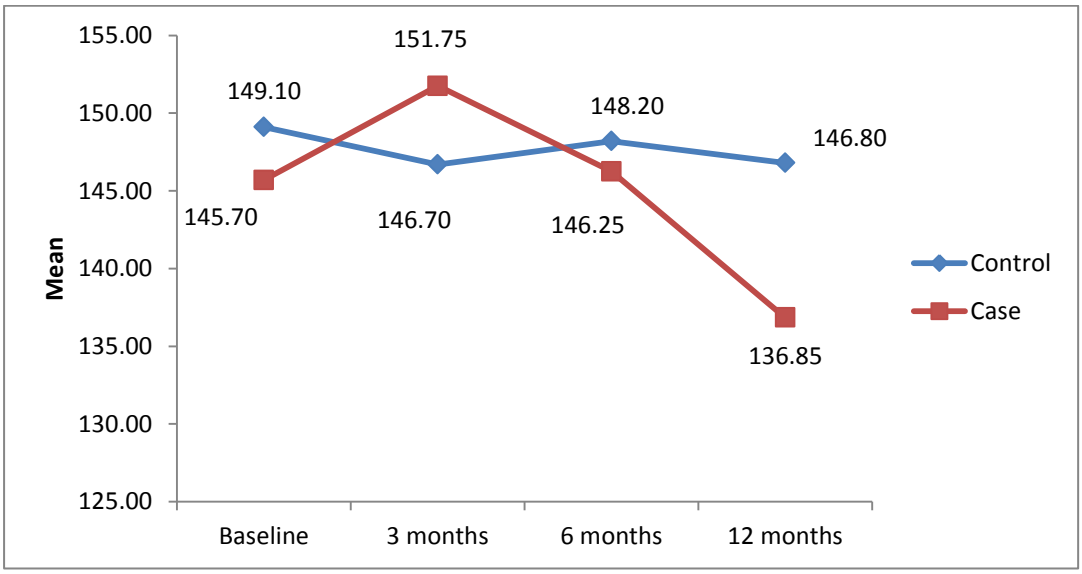


TABLE 98: COMPARISON OF THE MEAN SERUM ALKALINE PHOSPHATASE VALUE OF CKD5D

TABLE 99: COMPARISON OF THE MEAN PTH VALUES OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
iPTH pg/ml baseline	195.50	19.45	195.65	15.68	-0.027	0.979	-0.15	5.59
iPTH at 3 months	195.55	14.81	195.15	15.39	0.084	0.934	0.40	4.78
iPTH at 6 months	198.25	10.77	195.55	15.13	0.650	0.519	2.70	4.15
iPTH at 12 months	193.55	11.17	187.35	16.07	1.417	0.165	6.20	4.38

There was statistically no difference in mean PTH level at baseline, 3, 6 and 12 months between control and case group. PTH values were195.50, 195.55, 198.25, 193.55, at baseline, 3, 6 and 12 months for controls. These were195.65, 195.15, 195.55, 187.35 at baseline, 3, 6 and 12 months for cases.

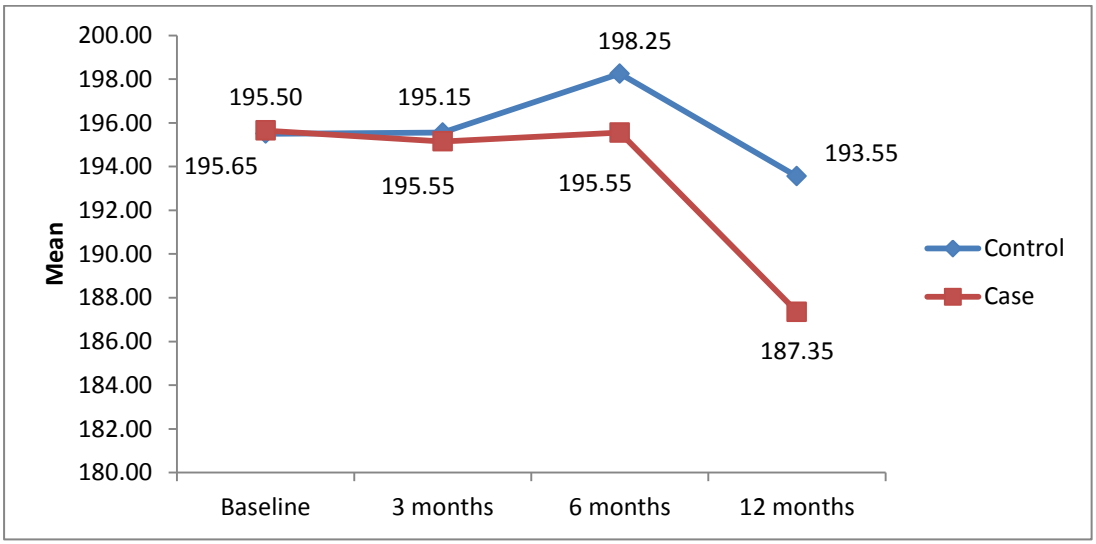


FIGURE 99: COMPARISON OF THE MEAN PTH VALUES OF CKD5D

TABLE 100: COMPARISON OF DIFFERENCE IN MEAN PTH VALUE OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-3m	-0.05	16.74	0.50	13.67	-0.114	0.910	-0.55	4.83
0-6m	-2.75	17.56	0.10	15.47	-0.545	0.589	-2.85	5.23
0-12m	1.95	17.87	8.30	18.90	-1.092	0.282	-6.35	5.82
3-6m	-2.70	9.04	-0.40	10.29	-0.751	0.457	-2.30	3.06
3-12m	2.00	14.44	7.80	13.90	-1.294	0.203	-5.80	4.48
6-12m	4.70	10.60	8.20	12.06	-0.975	0.336	-3.50	3.59

There was statistically no difference in change in the mean value of PTH at 3, 6 and 12 months between control and case group.

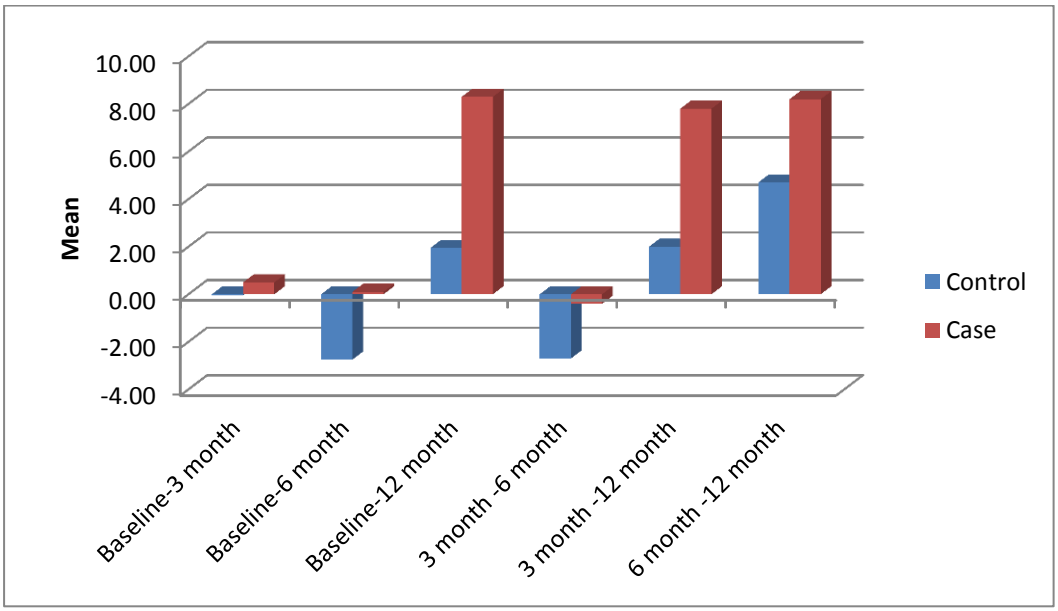


FIGURE 100: COMPARISON OF DIFFERENCE IN MEAN PTH VALUE OF CKD5D

TABLE 101: COMPARISON OF THE MEAN VITAMIN D3 VALUES OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Vitamin D3 ng/ml baseline	24.25	4.66	24.95	3.61	-0.532	0.598	-0.70	1.32
Vitamin D3 at 3 months	26.50	3.20	25.90	2.81	0.630	0.533	0.60	0.95
Vitamin D3 at 6 months	25.85	3.84	25.95	3.07	-0.091	0.928	-0.10	1.10
Vitamin D3 at 12 months	26.20	3.00	23.70	4.09	2.203	0.034	2.50	1.13

There was no difference in mean vitamin D3 level at baseline, 3 and 6 months between control and case group. But difference at 12 month was significant. The mean vitamin D3 was 24.25, 26.50, 25.85, 26.20 at baseline, 3, 6 and 12 months for controls. This was 24.95, 25.90, 25.95, 23.70at baseline, 3, 6 and 12 months for cases.

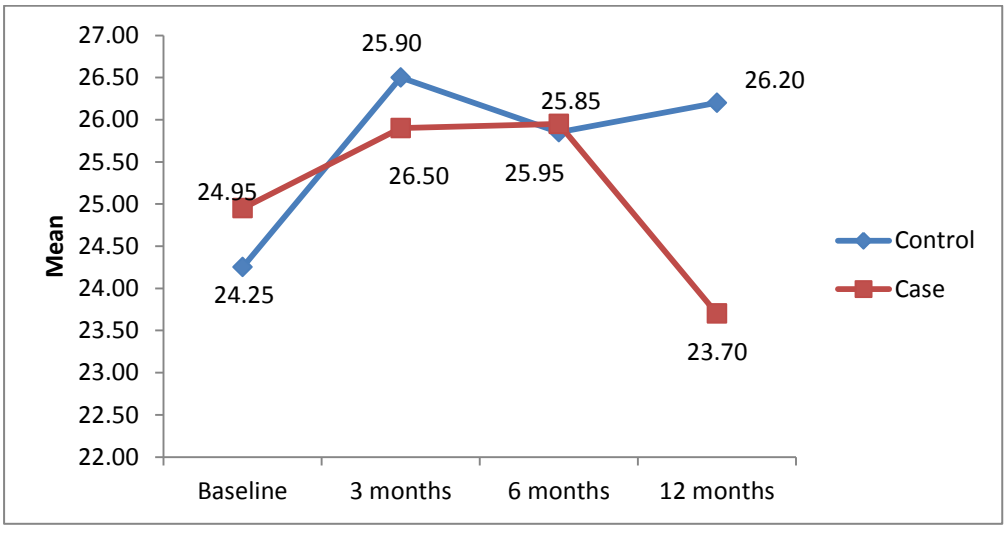


FIGURE 101: COMPARISON OF THE MEAN VITAMIN D3 VALUES OF CKD5D

TABLE 102: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF LUMBAR SPINE OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6M	0.15	0.23	-0.13	0.09	5.152	0.000	0.29	0.06
0-12M	0.28	0.30	-0.30	0.20	7.093	0.000	0.58	0.08

Mean lumbar spine T score was -1.38 for case and -1.86 for control respectively at baseline. It was -1.25 and -2.02 for case and control respectively at 6 months. It was -1.07 and -2.14 for case and control respectively at 12 months. There was improvement in mean T score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean T score was statistically significant between two groups at 6 and 12 month.

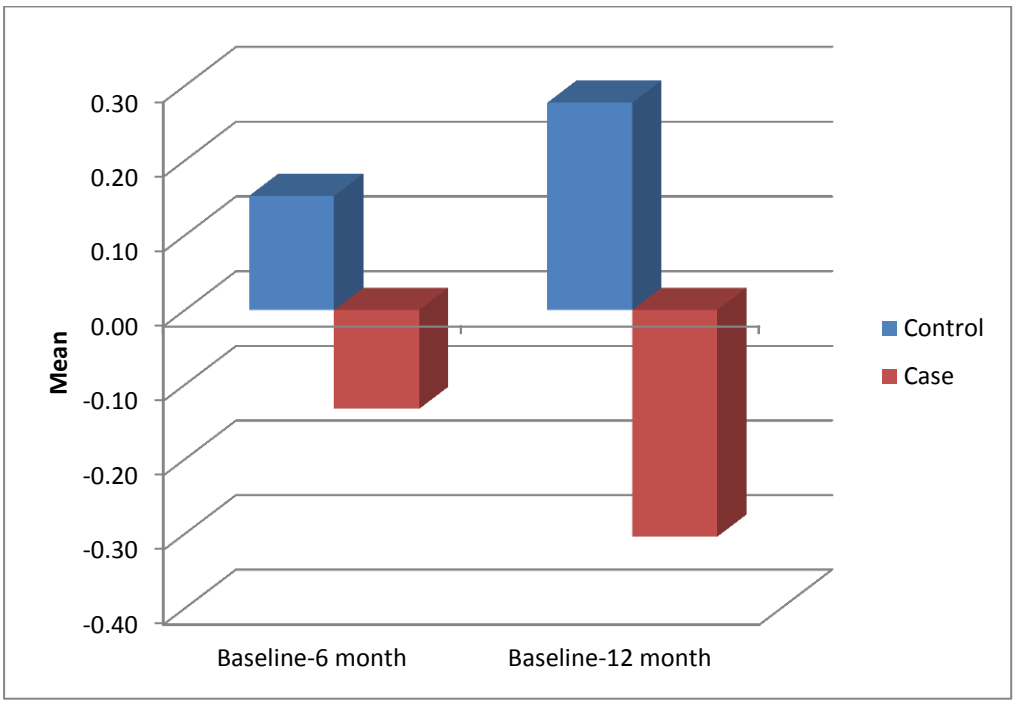


FIGURE 102: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF LUMBAR SPINE OF CKD5D

TABLE 103: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF LUMBAR SPINE OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6M	0.08	0.07	-0.12	0.06	9.313	0.000	0.20	0.02
0-12M	0.14	0.11	-0.31	0.38	5.133	0.000	0.45	0.09

Mean lumbar spine Z score was -0.51for case and -0.64 for control respectively at baseline. It was -0.39 and -0.72 for case and control respectively at 6 months. It was -0.20 and -0.78for case and control respectively at 12 months.

There was improvement in mean Z score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean Z score was statistically significant between two groups at 6 and 12 month.

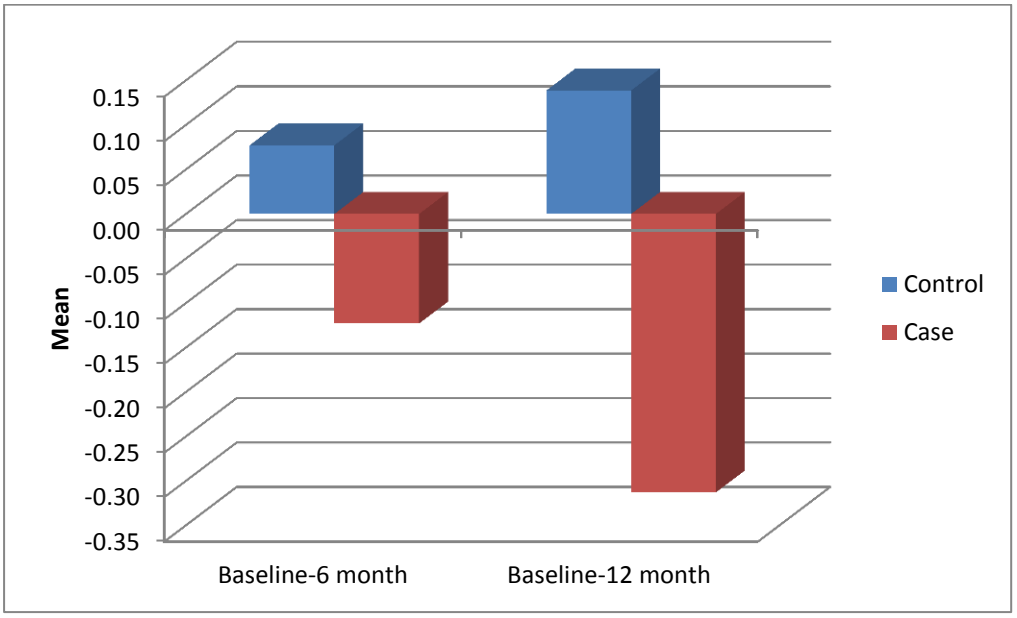


FIGURE 103: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF LUMBAR SPINE OF CKD5D

TABLE 104: COMPARISON OF MEAN BMD AT LEVEL OF LUMBAR SPINE OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline g/cm2	1.09	0.26	1.08	0.20	0.133	0.895	0.01	0.07
At 6 month	1.04	0.24	1.17	0.21	-1.766	0.085	-0.13	0.07
At 12month	0.96	0.22	1.26	0.22	-4.490	0.000	-0.31	0.07
0-6M	0.05	0.04	-0.09	0.08	6.725	0.000	0.14	0.02
0-12M	0.13	0.11	-0.18	0.12	8.732	0.000	0.32	0.04

Mean lumbar spine BMD was 1.08 for case and 1.09 for control respectively at baseline. It was 1.17 and 1.04 for case and control respectively at 6 months. It was 1.26 and 0.96for case and control respectively at 12 month.

There was improvement in mean BMD at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in BMD at 12 month was statistically significant between two groups. This difference in change in mean BMD was statistically significant between two groups at 6 and 12 month.

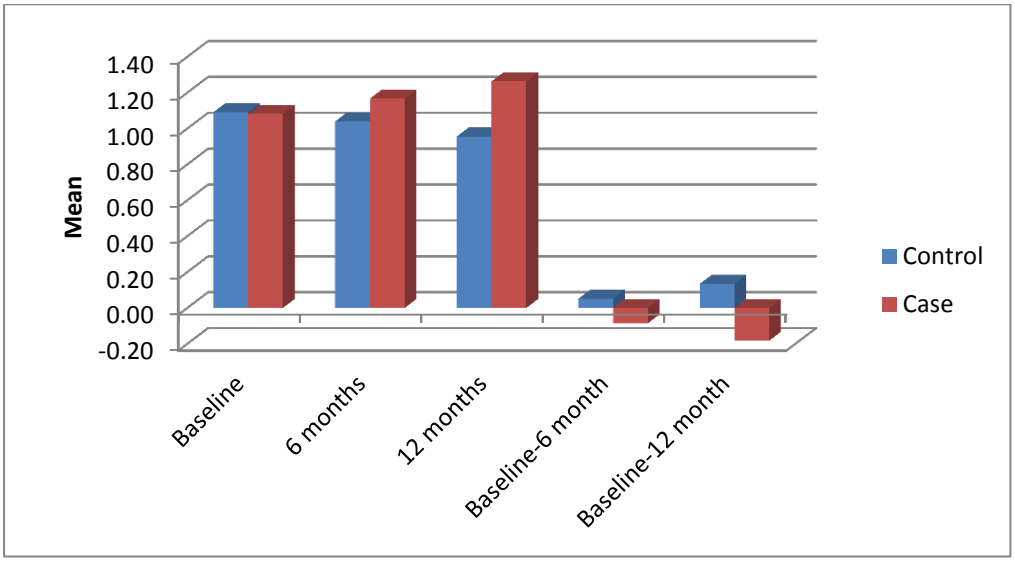


FIGURE 104: COMPARISON OF MEAN BMD AT LEVEL OF LUMBAR SPINE OF CKD5D

TABLE 105: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF FEMUR NECK OF CKD 5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6M	0.09	0.17	-0.19	0.17	5.249	0.000	0.28	0.05
0-12M	0.24	0.25	-0.39	0.18	9.305	0.000	0.63	0.07

Mean femur neck T score was -2.19 for case and -2.12 for control respectively at baseline. It was -1.99 and -2.21 for case and control respectively at 6 months. It was -1.79 and -2.36 for case and control respectively at 12 month.

There was improvement in mean T score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean T score was statistically significant between two groups at 6 and 12 month.

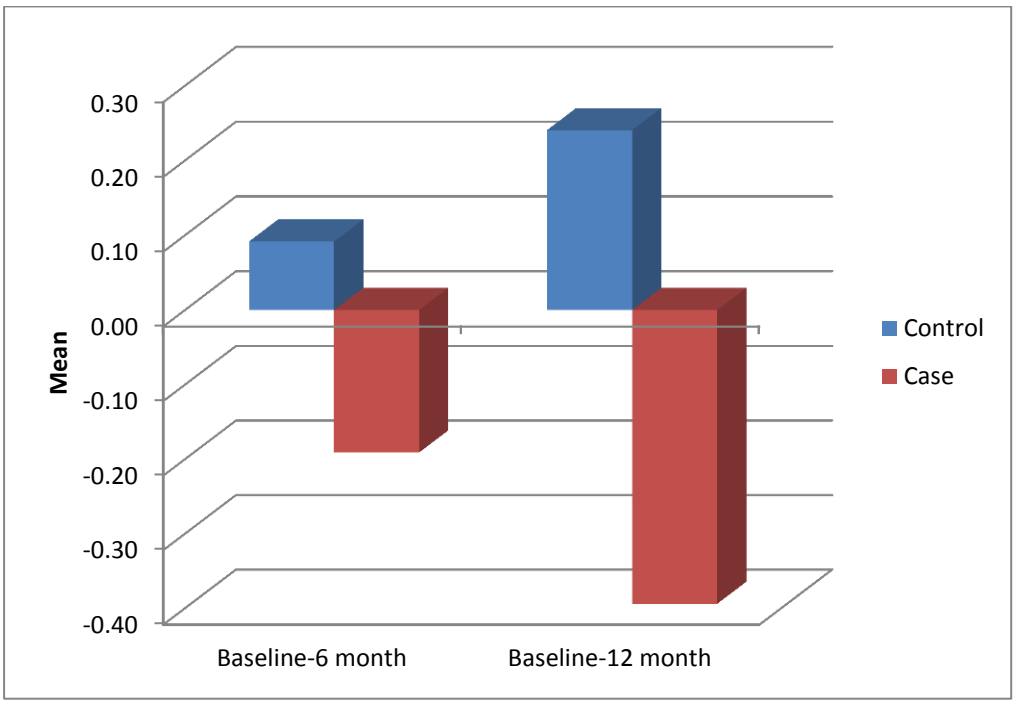


FIGURE 105: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE AT LEVEL OF FEMUR NECK OF CKD5D

TABLE 106: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF FEMUR NECK OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6M	0.06	0.09	-0.08	0.10	4.813	0.000	0.15	0.03
0-12M	0.16	0.13	-0.21	0.14	8.647	0.000	0.38	0.04

Mean femur neck Z score was -0.49 for case and -0.63 for control respectively at baseline. It was -0.40 and -0.69 for case and control respectively at 6 months. It was -0.27 and -0.79 for case and control respectively at 12 months.

There was improvement in mean Z score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean T score was statistically significant between two groups at 6 and 12 month.

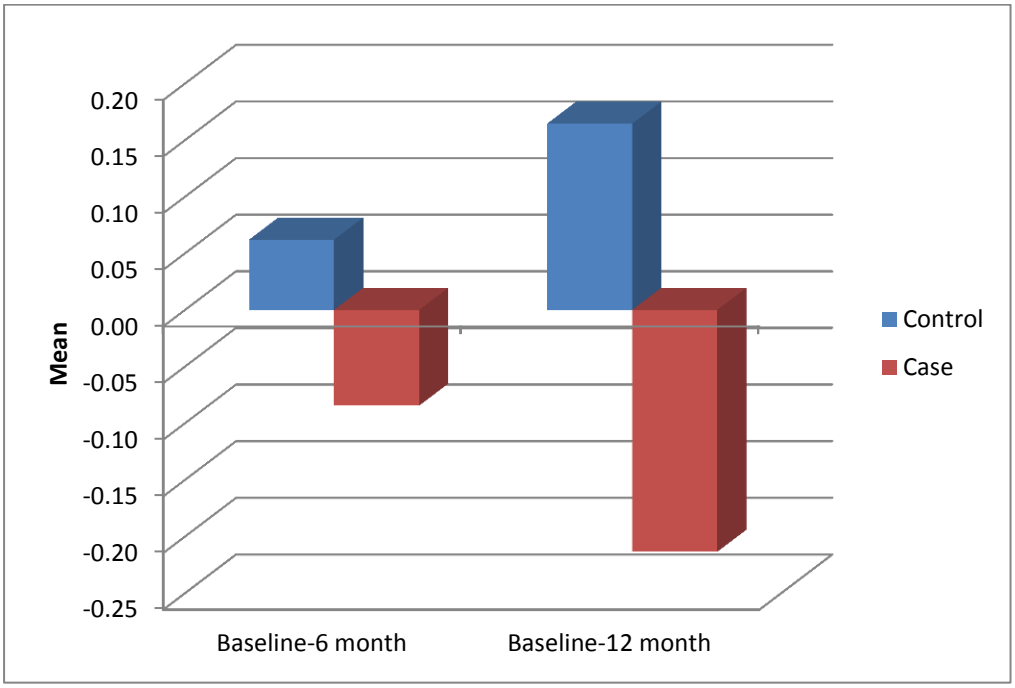


FIGURE 106: COMPARISON OF THE DIFFERENCE OF MEAN Z SCORE AT LEVEL OF FEMUR NECK OF CKD5D

TABLE 107: COMPARISON OF MEAN BMD AT LEVEL OF FEMUR NECK OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline g/m2	0.86	0.19	0.82	0.27	0.497	0.622	0.04	0.07
At 6 month	0.81	0.21	0.89	0.27	-1.018	0.315	-0.08	0.08
At 12 month	0.75	0.21	0.99	0.29	-3.033	0.004	-0.24	0.08
DIFFERENCE 0- 6M	0.05	0.04	-0.07	0.05	8.036	0.000	0.11	0.01
DIFFERENCE 0-12M	0.10	0.08	-0.17	0.10	9.773	0.000	0.28	0.03

Mean femur neck BMD was 0.82 for case and 0.86 for control respectively at baseline. It was 0.89 and 0.81 for case and control respectively at 6 months. It was 0.99 and 0.75for case and control respectively at 12 month.

There was improvement in mean BMD at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in BMD at 12 month was statistically significant between two groups. This difference in change in mean BMD was statistically significant between two groups at 6 and 12 month.

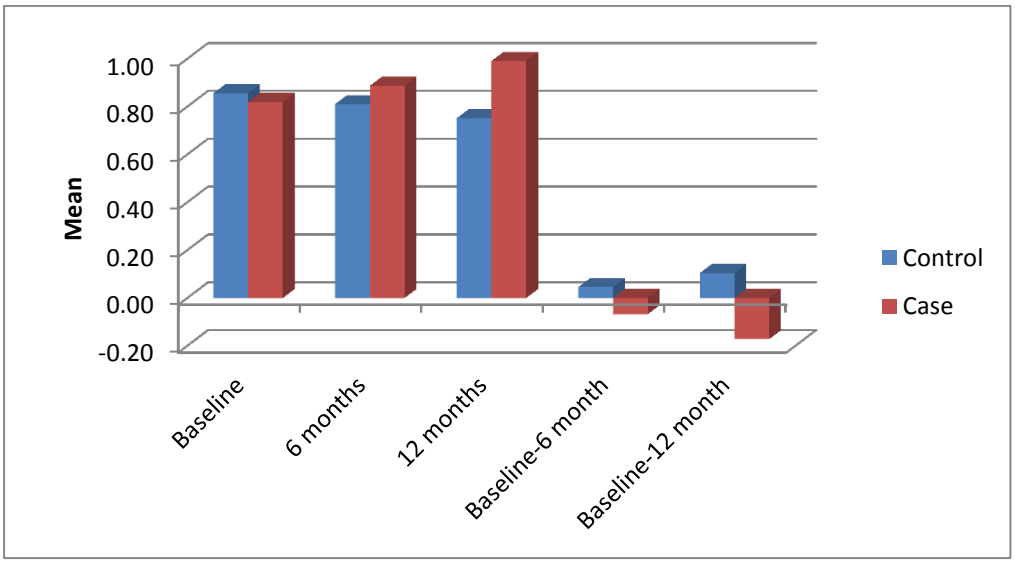


FIGURE 107: COMPARISON OF MEAN BMD AT LEVEL OF FEMUR NECK OF CKD5D

TABLE 108: COMPARISON OF THE DIFFERENCE OF MEAN T SCORE OF TOTAL HIP OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0- 6M	0.13	0.09	-0.18	0.11	9.407	0.000	0.31	0.03
0-12M	0.28	0.29	-0.35	0.16	8.463	0.000	0.62	0.07

Mean total hip T score was -2.10 for case and -1.81 for control respectively at baseline. It was -1.91 and -1.94 for case and control respectively at 6 months. It was -1.75 and -2.09for case and control respectively at 12 month.

There was improvement in mean T score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in change in mean T score was statistically significant between two groups at 6 and 12 month.

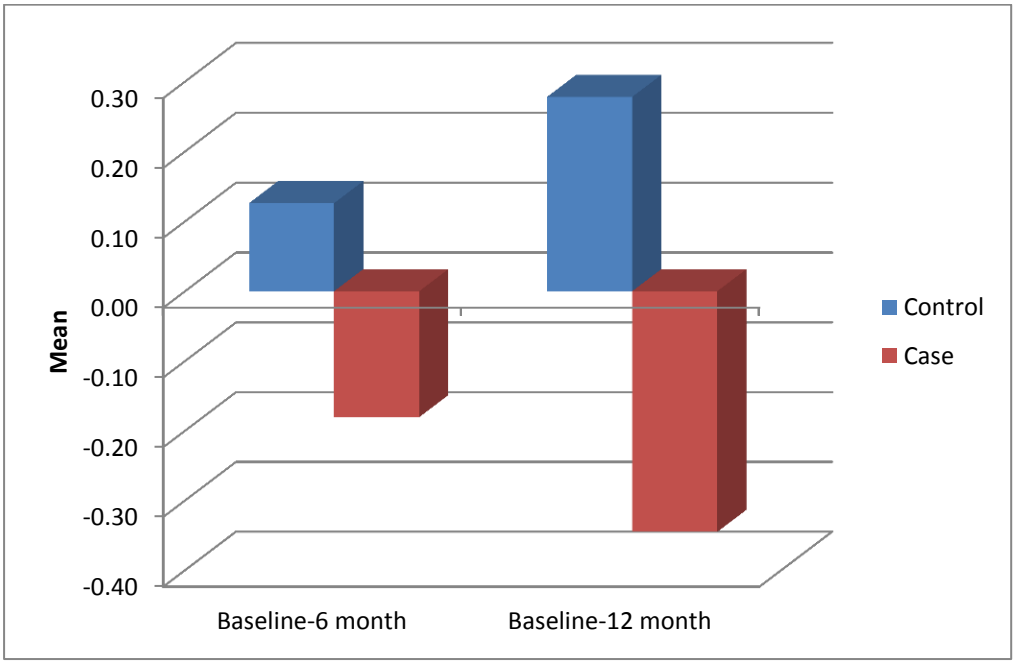


FIGURE 108: COMPARISON OFTHE DIFFERENCE OF MEAN T SCORE OF TOTAL HIP OF CKD5D

TABLE 109: COMPARISON OFTHE DIFFERENCE OF MEAN Z SCORE OF TOTAL HIP OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
0-6 M	0.10	0.09	-0.16	0.16	6.415	0.000	0.26	0.04
0-12 M	-0.08	0.95	-0.48	0.74	1.462	0.152	0.40	0.27

Mean total hip Z score was -1.19 for case and -0.58 for control respectively at baseline. It was -0.91 and -0.68 for case and control respectively at 6 months. It was -0.02 and -0.50 for case and control respectively at 12 months.

There was improvement in mean Z score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in change in mean Z score was statistically significant between two groups at 6 month.

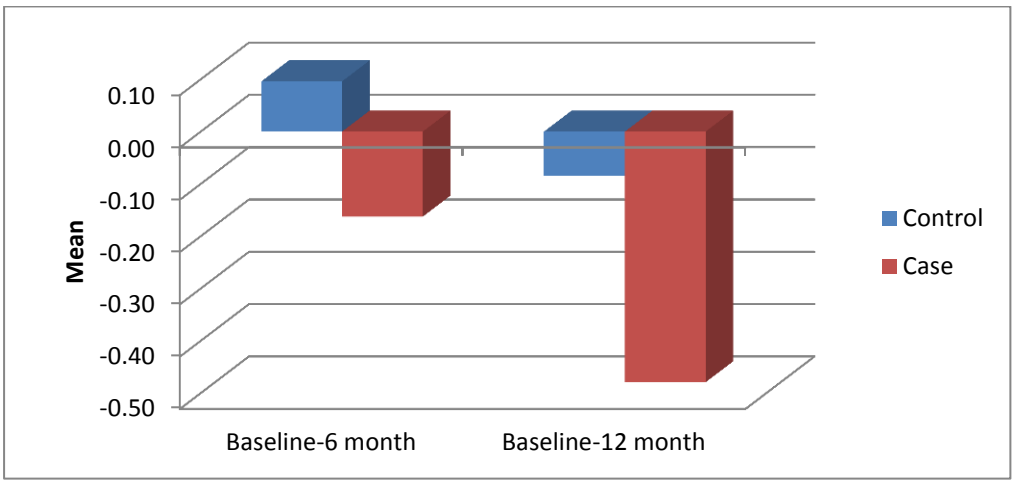


FIGURE 109: COMPARISON OFTHE DIFFERENCE OF MEAN Z SCORE OF TOTAL HIP OF CKD5D

TABLE 110: COMPARISON OF MEAN BMD OF TOTAL HIP OF CKD5D

CKD 5D stage	Control		Case		t	p-value	Difference	
	Mean	SD	Mean	SD			Mean	SD
Baseline g/cm2	0.91	0.24	0.80	0.12	1.800	0.080	0.11	0.06
At 6 month	0.82	0.20	0.90	0.16	-1.391	0.172	-0.08	0.06
At 12 month	0.76	0.18	1.03	0.24	-4.131	0.000	-0.27	0.07
DIFFERENCE 0-6M	0.09	0.07	-0.10	0.08	7.796	0.000	0.19	0.02
DIFFERENCE 0-12 M	0.15	0.09	-0.22	0.18	8.532	0.000	0.38	0.04

Mean total hip BMD was 0.80 for case and 0.91 for control respectively at baseline. It was 0.90 and 0.82 for case and control respectively at 6 months. It was 1.03 and 0.76 for case and control respectively at 12 month. The difference in BMD between two groups was statistically significant at 12 month.

There was improvement in mean BMD at level of total hip at 6 and 12 month in patients, who received oral alendronate compared to controls. This difference in change in mean BMD was statistically significant between two groups at 6 and 12 month.

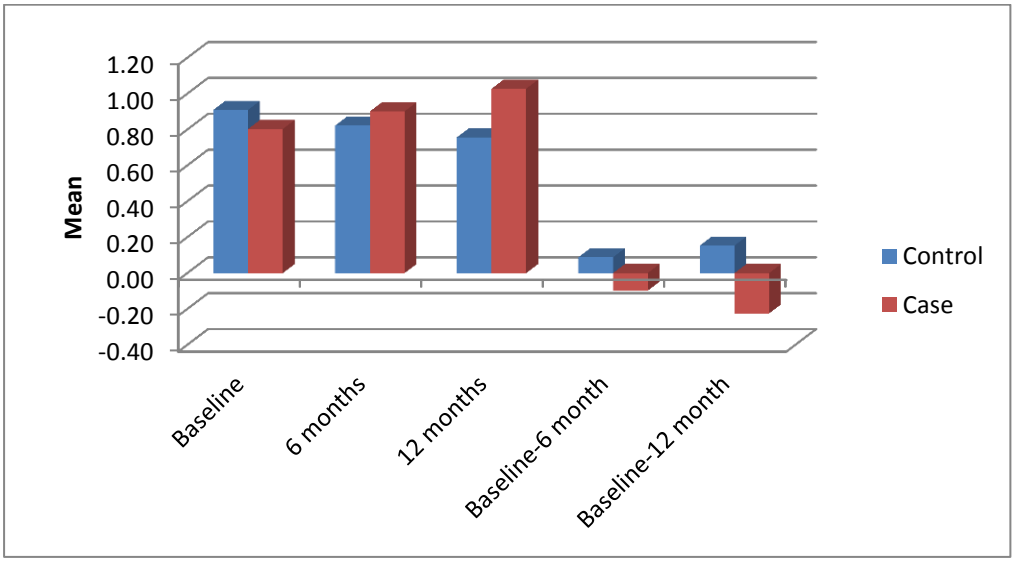


FIGURE 110: COMPARISON OF MEAN BMD OF TOTAL HIP OF CKD5D

TABLE 111: COMPARISON OF SUBPERIOSTEAL RESORPTION OF PHALENGES OF ON X RAY OF HAND

		Control		Case		Total	Chi-square value	p-value
Sub periosteal resorbtion of phalanges on x-ray hand	Yes	4	10.0%	2	5.0%	6	0.721	0.396
	No	36	90.0%	38	95.0%	74		

Only 2 patients (CKD5D) who received oral alendronate had evidence of sub periosteal resorption of phalanges on X ray hand compared to 4 patients (CKD5D=3, CKD5=1), who did not receive alendronate.

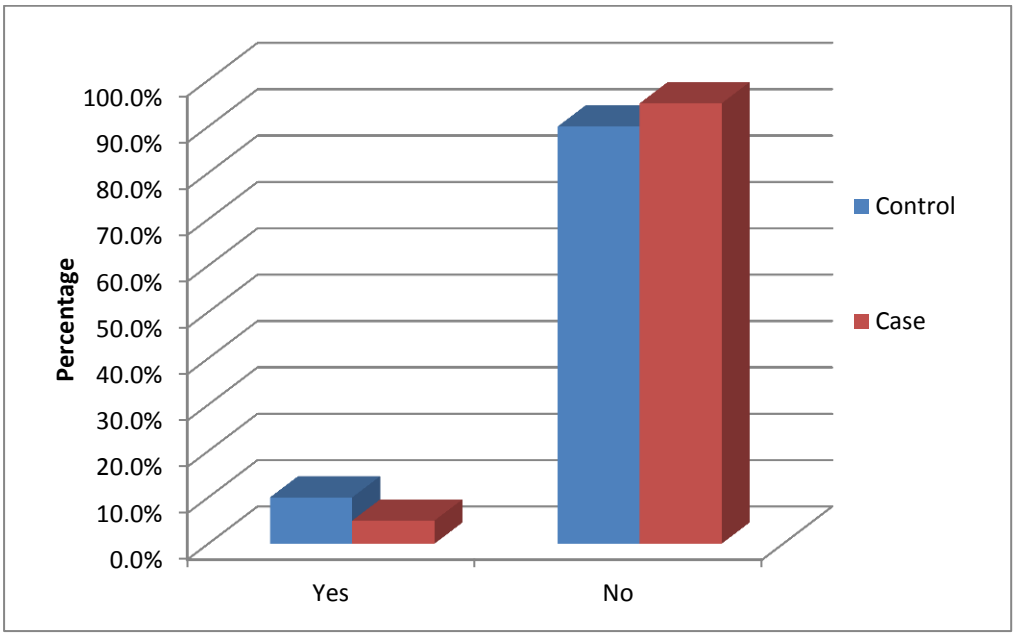


FIGURE 111: COMPARISON OF SUBPERIOSTEAL RESORBTION OF PHALENGES OF ON X RAY OF HAND

TABLE 112: COMPARISON OF ABDOMINAL AORTA CALCIFICATION ON LATERAL X RAY OF LUMBAR SPINE

						Total	Chi-square value	p-value
		Control		Case				
Calcification of abdominal aorta on x ray of lumbar spine	Yes	5	12.5%	2	5.0%	7	1.409	0.235
	No	35	87.5%	38	95.0%	73		

Only 2 patients (CKD5D) who received oral alendronate had evidence abdominal aorta calcification on lateral X ray of lumbar spine compared to 5 patients (CKD5D=4, CKD5=1), who did not receive alendronate.

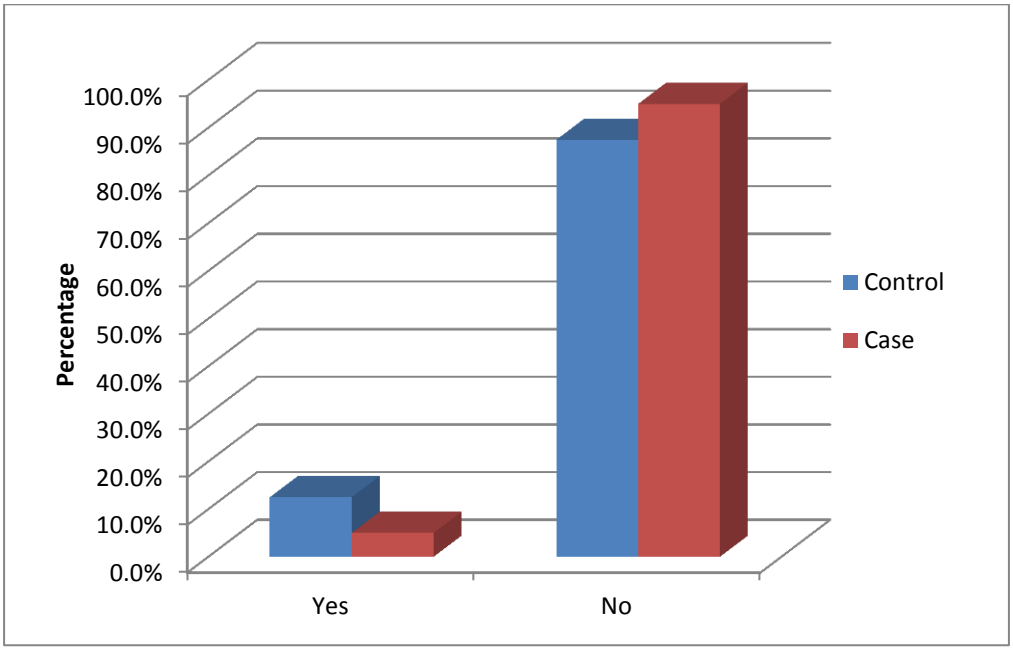


FIGURE 112: COMPARISON OF ABDOMINAL AORTA CALCIFICATION ON LATERAL X RAY OF LUMBAR SPINE

TABLE 113: COMPARISON OF FRACTURES BETWEEN TWO GROUPS

						Total
		Control	**Control (%)**	**Case**	**Case (%)**	
Fracture at X-ray DL spine at baseline	No	38	95.0%	39	97.5%	77
	Yes	2	5.0%	1	2.5%	3

Two patients in control group and one in case group had fracture on x ray of DL spine.

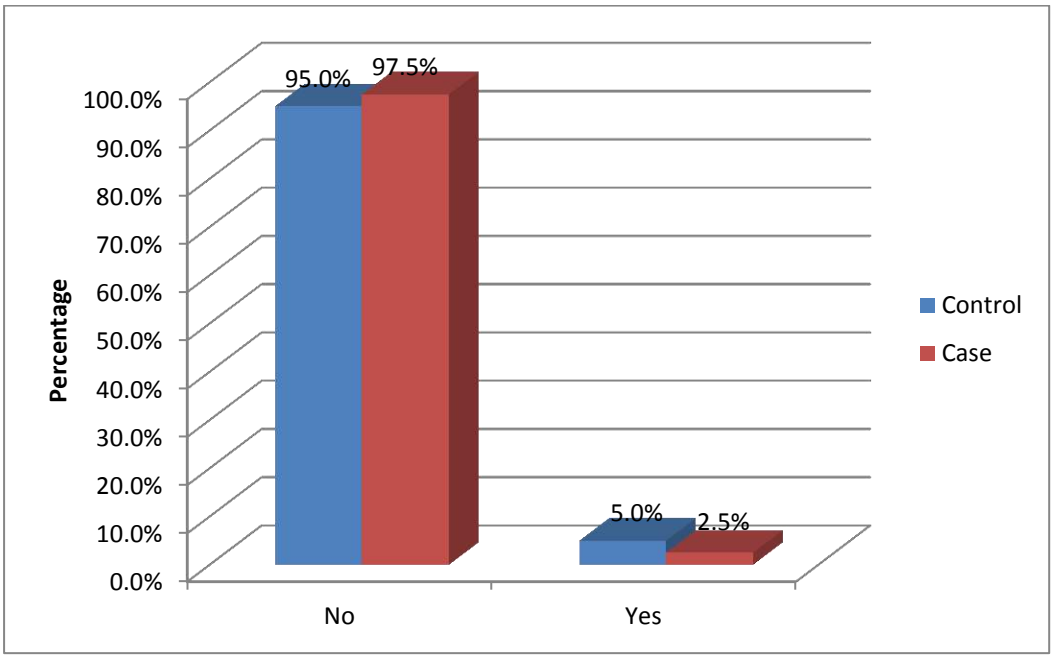


FIGURE 113: COMPARISON OF FRACTURES BETWEEN TWO GROUPS

TABLE 114: COMPLICATIONS OF ORAL ALENDRONATE TREATMENT

GI adverse events	Cardiovascular adverse events	Osteonecrosis	Dermatological manifestations	Others	Hospitalization	Death
5	0	1	1	1	0	0
12.5%	0.0%	2.5%	2.5%	2.5%	0.0%	0.0%

Five patients had initially GI intolerance to alendronate, one had osteonecrosis of jaw, one had dermatological reaction to alendronate, but none of them required stoppage of drug due to side effects.

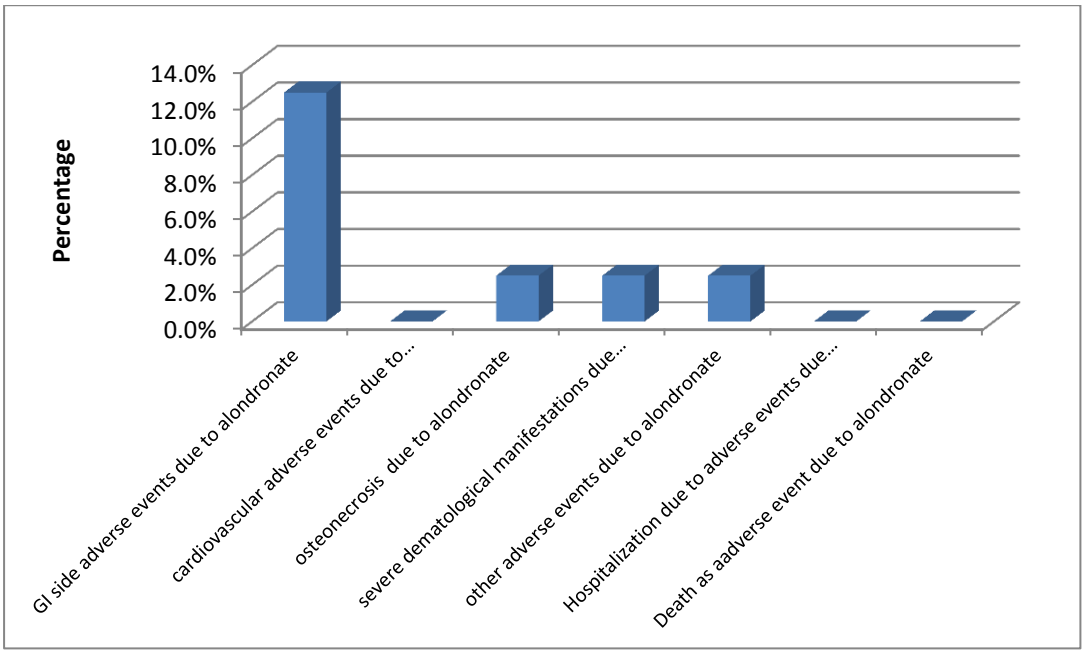


FIGURE 114: COMPLICATIONS OF ORAL ALENDRONATE TREATMENT

TABLE 115: COMPARISON OF DIFFERENCE IN SERUM CREATININE AMONG VARIOUS CKD SUBGROUPS

	STAGE 3	STAGE 4	STAGE 5	STAGE 5D
0-3m	0.11	-0.98	-0.39	-0.22
0- 6m	-0.09	-0.97	-0.79	-0.22
0-12m	-0.34	-0.95	-1.27	-0.38
Difference 3-6m	-0.20	0.01	-0.39	0.00
Difference 3-12m	-0.46	0.03	-0.88	-0.16
Difference 6-12m	-0.26	0.02	-0.49	-0.16

There was statistically no significant difference when change in mean serum creatinine level was compared within various CKD subgroups at 6 and 12 months.

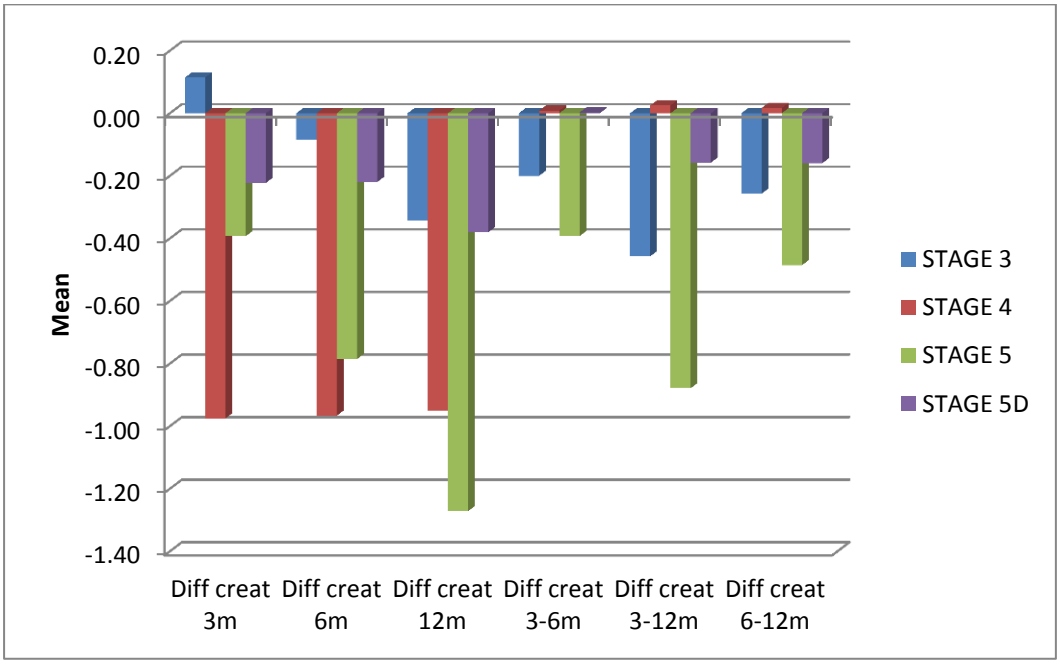


FIGURE 115: COMPARISON OF DIFFERENCES IN SERUM CREATININE AMONG VARIOUS CKD SUBGROUPS

TABLE 116: COMPARISON OF DIFFERENCES IN MEAN PTH LEVEL AMONG VARIOUS CKD SUB-GROUPS

	STAGE 3	STAGE 4	STAGE 5	STAGE 5D
0- 3m	2.00	3.33	0.36	0.23
0- 6m	1.86	4.50	7.21	-1.33
0-12m	12.00	15.25	16.36	5.13
3-6m	-0.14	1.17	6.86	-1.55
3-12m	10.00	11.92	16.00	4.90
6-12m	10.14	10.75	9.14	6.45

There was statistically no significant difference when change in mean PTH level was compared within various CKD subgroups at 6 and 12 month.

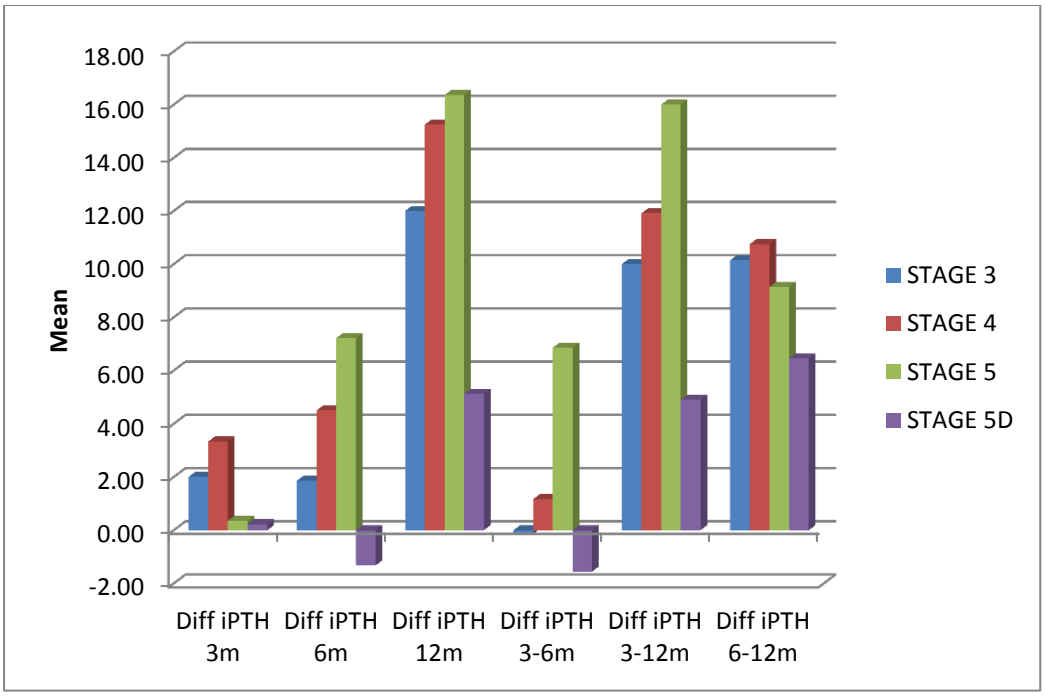


FIGURE 116: COMPARISON OF DIFFERENCES IN MEAN PTH LEVEL AMONG VARIOUS CKD SUB-GROUPS

TABLE 117: COMPARISON OF DIFFERENCES IN T SCORE AT LUMBAR SPINE AMONG VARIOUS CKD SUBGROUPS

	STAGE 3	STAGE 4	STAGE 5	STAGE 5D
0- 6M	-0.02	-0.03	-0.05	0.01
0-12M	0.02	-0.03	-0.09	-0.01

There was statistically no significant difference when change in mean Lumbar spine T score was compared within various CKD subgroups at 6 and 12 months.

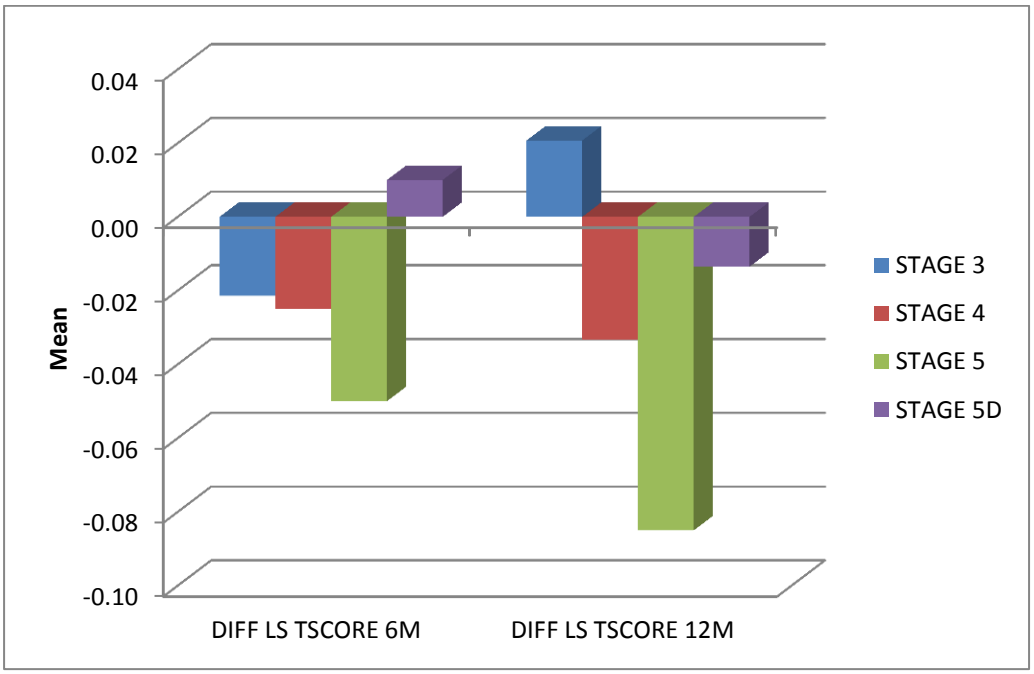


FIGURE 117: COMPARISON OF DIFFERENCES IN T SCORE AT LUMBAR SPINE AMONG VARIOUS CKD SUB-GROUPS

TABLE 118: COMPARISON OF DIFFERENCES IN Z SCORE AT LUMBAR SPINE AMONG VARIOUS CKD SUB-GROUPS

	STAGE 3	STAGE 4	STAGE 5	STAGE 5D
0-6M	-0.04	0.00	-0.05	-0.02
0-12M	-0.03	-0.05	-0.10	-0.09

There was statistically no significant difference when change in mean Lumbar spine Z score was compared within various CKD subgroups at 6 and 12 months.

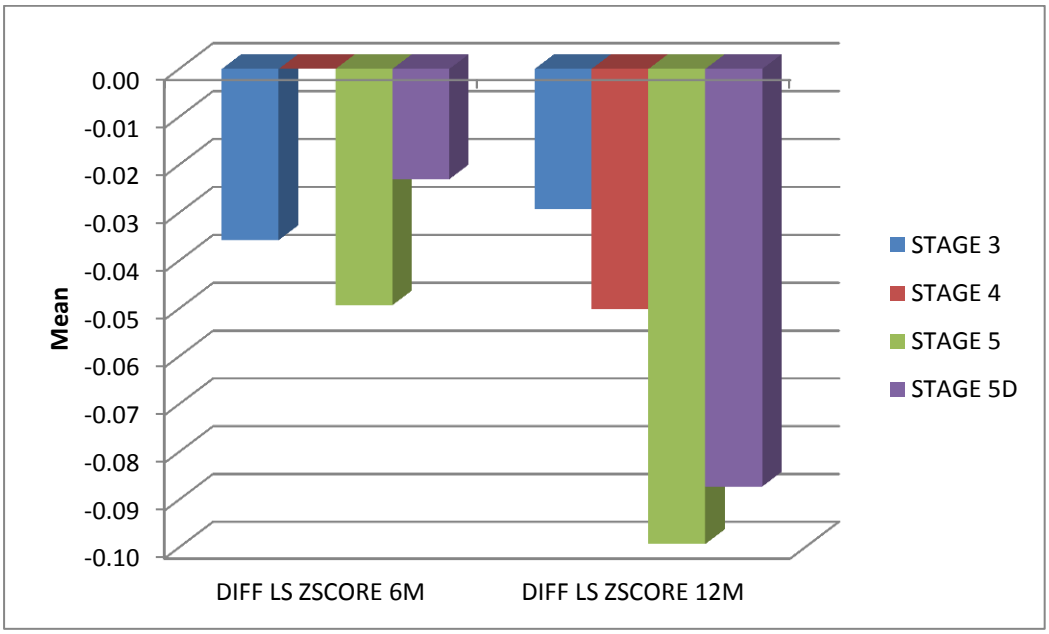


FIGURE 118: COMPARISON OF DIFFERENCES IN Z SCORE AT LUMBAR SPINE AMONG VARIOUS CKD SUB-GROUPS

TABLE 119: COMPARISON OF DIFFERENCES IN BMD AT LUMBAR SPINE AMONG VARIOUS CKD SUB-GROUPS

	STAGE 3	STAGE 4	STAGE 5	STAGE 5D
0- 6M	-0.06	0.00	-0.03	-0.02
0- 12M	-0.08	-0.01	-0.08	-0.02

There was no statistically significant difference when change in mean Lumbar spine BMD was compared within various CKD subgroups at 6 and 12 months.

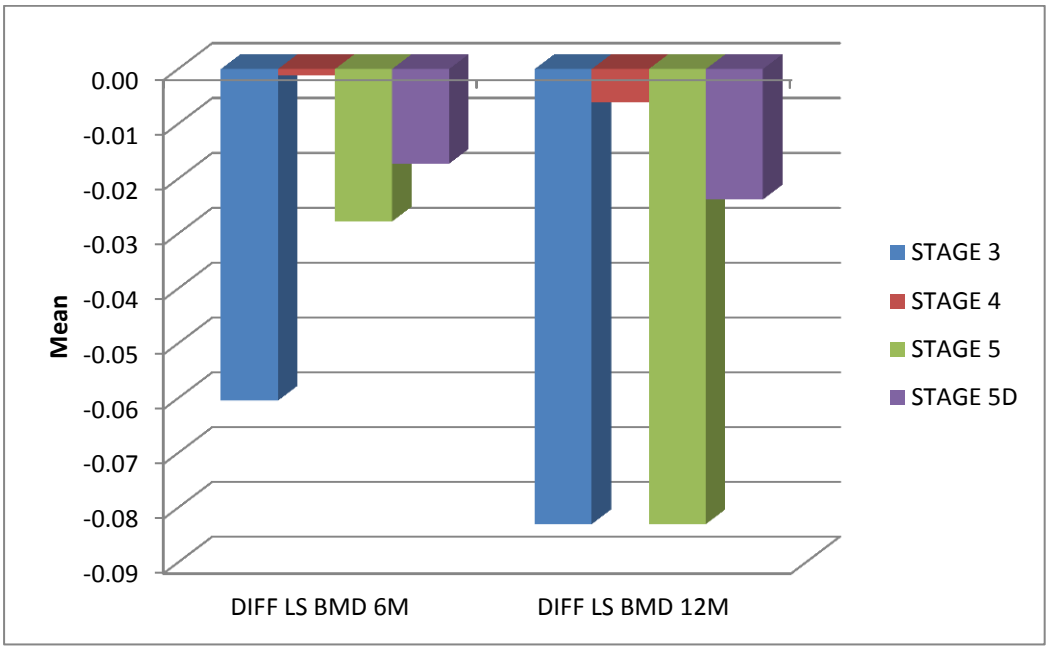


FIGURE 119: COMPARISON OF DIFFERENCE IN BMD AT LUMBAR SPINE AMONG VARIOUS CKD SUB-GROUPS

TABLE 120: COMPARISON OF DIFFERENCES IN T SCORE AT FEMUR NECK AMONG VARIOUS CKD SUB-GROUPS

	STAGE 3	STAGE 4	STAGE 5	STAGE 5D
0- 6M	-0.06	-0.10	-0.08	-0.05
0-12M	-0.13	-0.13	-0.16	-0.08

There was no statistically significant difference when change in mean femur neck T score was compared within various CKD subgroups at 6 and 12 months.

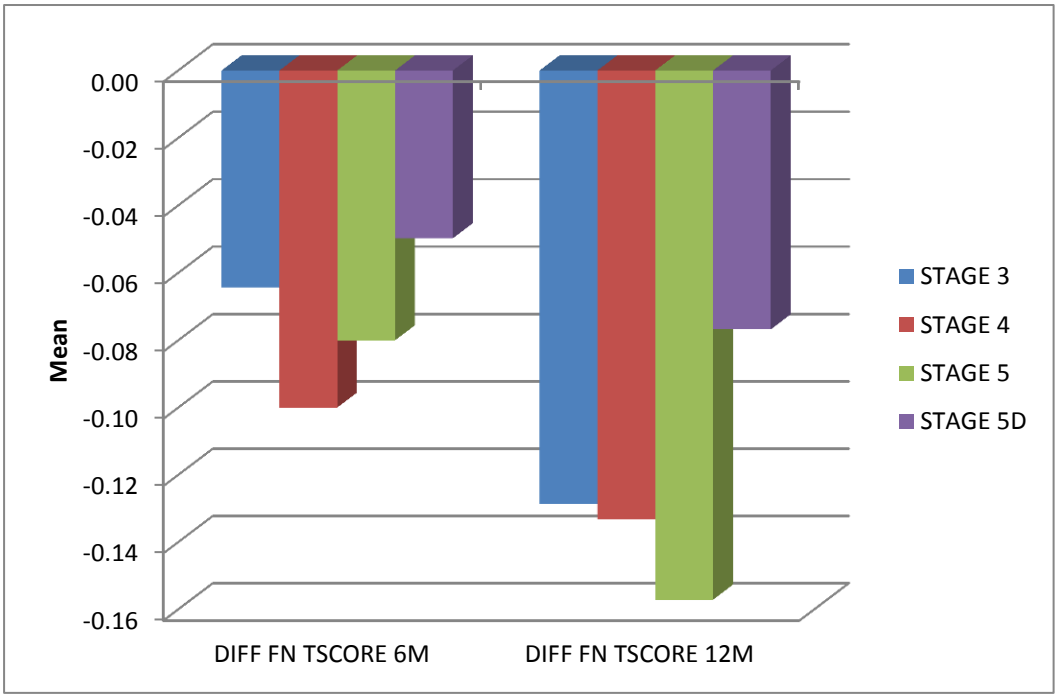


FIGURE 120: COMPARISON OF DIFFERENCES IN T SCORE AT FEMUR NECK AMONG VARIOUS CKD SUB-GROUPS

TABLE 121: COMPARISON OF DIFFERENCE IN Z SCORE AT FEMUR NECK AMONG VARIOUS CKD SUB-GROUPS

	STAGE 3	STAGE 4	STAGE 5	STAGE 5D
0- 6M	-0.01	-0.03	-0.06	-0.01
0- 12M	-0.03	-0.04	-0.10	-0.02

There was no statistically significant difference when change in mean femur neck Z score was compared within various CKD subgroups at 6 and 12 months.

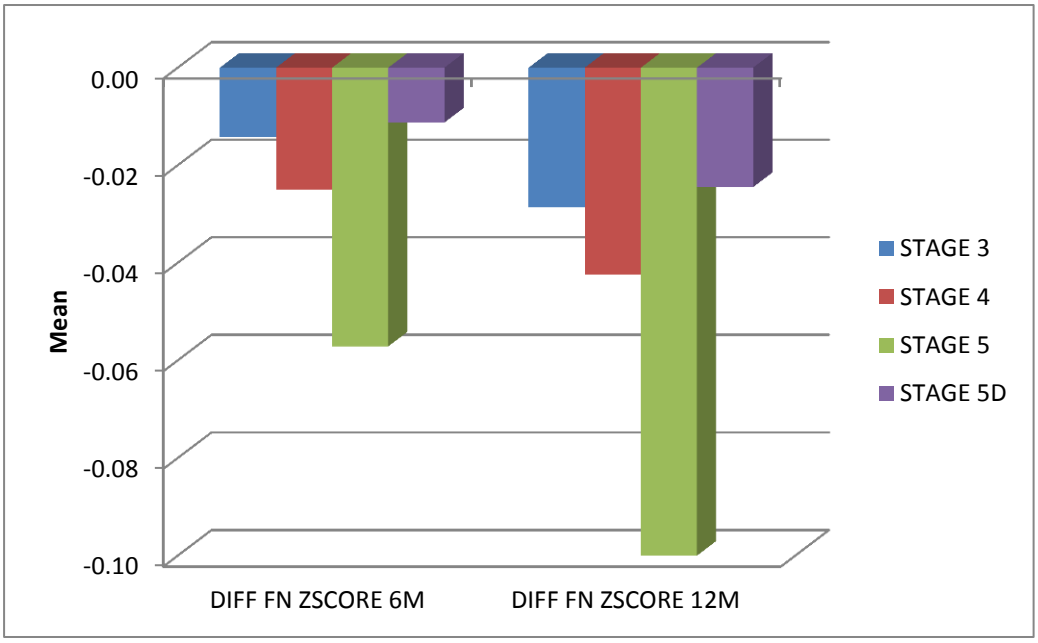


FIGURE 121: COMPARISON OF DIFFERENCE IN Z SCORE AT FEMUR NECK AMONG VARIOUS CKD SUB-GROUPS

TABLE 122: COMPARISON OF DIFFERENCE IN THE MEAN BMD AT FEMUR NECK AMONG VARIOUS CKD SUB-GROUPS

	STAGE 3	STAGE 4	STAGE 5	STAGE 5D
0- 6M	0.01	0.01	-0.05	-0.01
0- 12M	-0.15	-0.02	-0.09	-0.03

There was no statistically significant difference when change in mean femur neck BMD was compared within various CKD subgroups at 6 and 12 months.

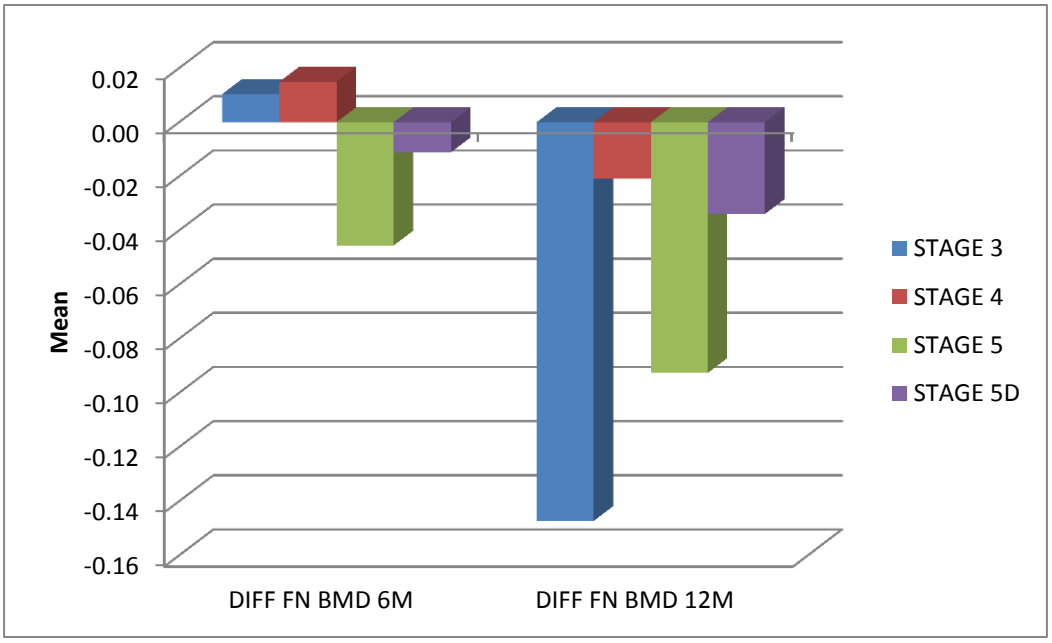


FIGURE 122: COMPARISON OF DIFFERENCE IN THE MEAN BMD AT FEMUR NECK AMONG VARIOUS CKD SUB-GROUPS

TABLE 123: COMPARISON OF DIFFERENCE IN T SCORE AT LEVEL OF HIP AMONG VARIOUS CKD SUB-GROUPS

	STAGE 3	STAGE 4	STAGE 5	STAGE 5D
DIFF TH TSCORE 6M	-0.04	-0.12	-0.02	-0.03
DIFF TH TSCORE 12M	-0.10	-0.21	-0.10	-0.03

There was no statistically significant difference when change in mean total hip T score was compared within various CKD subgroups at 6 and 12 months.

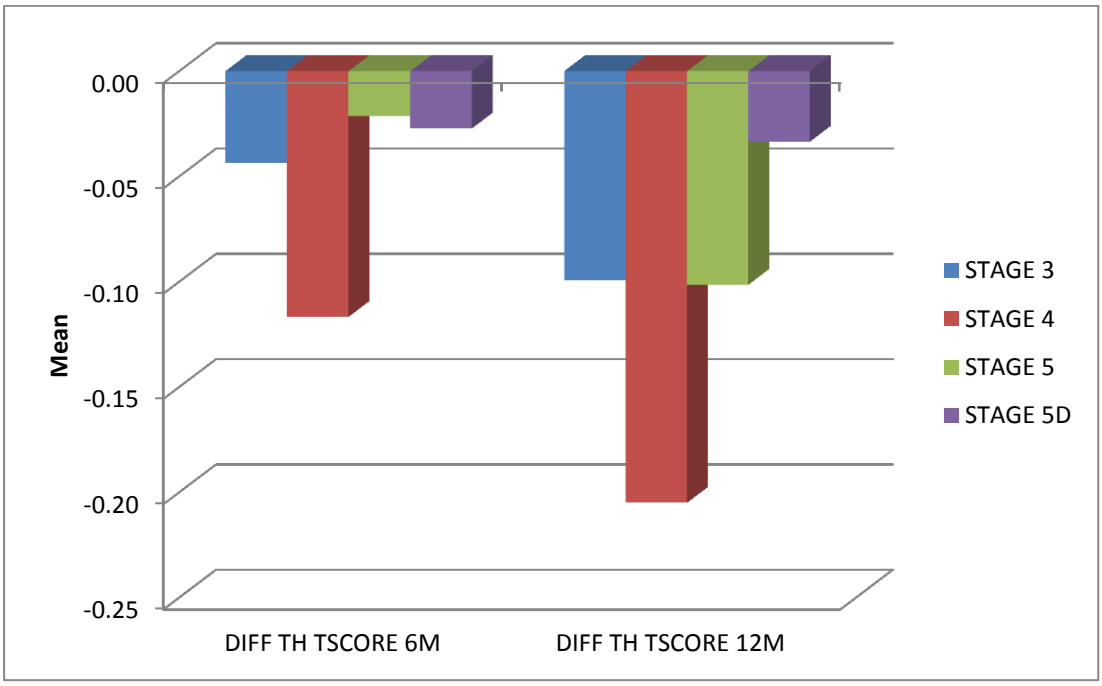


FIGURE 123: COMPARISON OF DIFFERENCE IN T SCORE AT LEVEL OF HIP AMONG VARIOUS CKD SUB-GROUPS

TABLE 124: COMPARISON OF DIFFERENCE IN Z SCORE AT LEVEL OF HIP AMONG VARIOUS CKD SUB-GROUPS

	STAGE 3	STAGE 4	STAGE 5	STAGE 5D
0- 6M	-0.03	-0.08	-0.06	-0.03
0-12M	-0.07	-0.17	-0.41	-0.28

There was no statistically significant difference when change in mean total hip Z score was compared within various CKD subgroups at 6 and 12 month

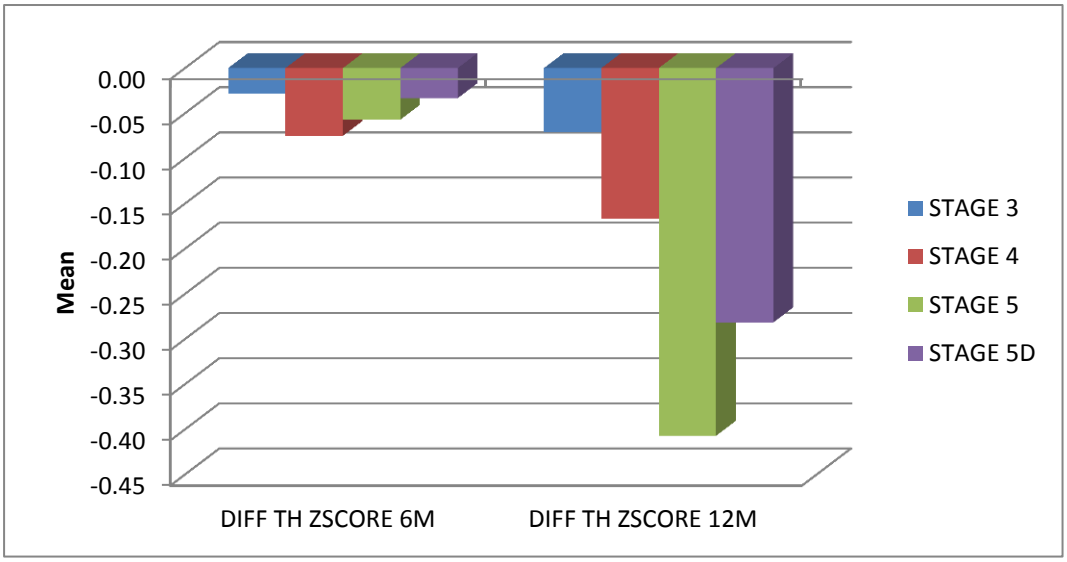


FIGURE 124: COMPARISON OF DIFFERENCE IN T SCORE AT LEVEL OF HIP AMONG VARIOUS CKD SUB-GROUPS

TABLE 125: COMPARISON OF DIFFERENCE BMD AT LEVEL OF HIP AMONG VARIOUS CKD SUB-GROUPS

	STAGE 3	STAGE 4	STAGE 5	STAGE 5D
0- 6M	-0.05	-0.02	-0.05	0.00
0-12 M	-0.08	-0.07	-0.09	-0.04

There was no statistically significant difference when change in mean total hip BMD was compared within various CKD subgroups at 6 and 12 months.

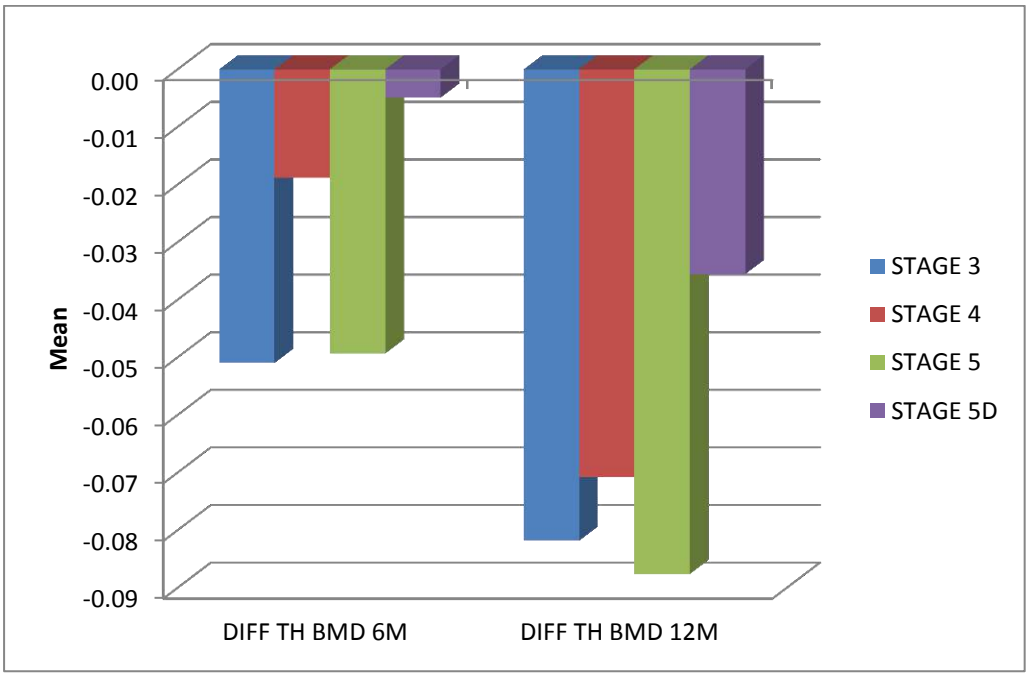


FIGURE 125: COMPARISON OF DIFFERENCE BMD AT LEVEL OF HIP AMONG VARIOUS CKD SUBGROUPS

DISCUSSION

Chronic kidney disease (CKD) may be an independent risk factor for bone loss and is common among older adults. Bisphosphonates are commonly used to reduce bone loss, but they are primarily cleared via renal excretion. Thus, in patients with severe renal impairment, bisphosphonate use has not been extensively investigated and either is not recommended (eg, risedronate, alendronate, ibandronate, tiludronate) or recommended only with precautions and careful monitoring (eg, etidronate, pamidronate). Bisphosphonate treatment, particularly at higher peak concentrations, may also contribute to deterioration of renal function and the efficacy of bisphosphonates for bone protection may be limited in patients with severe renal impairment or kidney failure. The evidence for patients with CKD is much less extensive. The large randomized trials excluded those with known renal failure, or with abnormal parathyroid hormone, calcium, or alkaline phosphatase.[6,17] Post hoc studies on the remaining subjects with an estimated glomerular filtration rate (eGFR) lower than 60 have shown that the fracture reduction was similar to rates in subjects with a normal eGFR. This is reassuring, because many patients with osteoporosis also have mild CKD, since both conditions increase with aging. However, important questions remain about the safety and efficacy of bisphosphonates in those with more advanced kidney disease. The objectives of this study were to evaluate efficacy and safety of bisphosphonates in subjects with various degrees of renal function impairment. The prospective case control study was done in patients with CKD stage 3-5D. The study period was from Feb 2018 to July 2019. A total of 150 patients of CKD age 3 -5D presenting to Nephrology ward, OPD and/or dialysis unit, of Dayanand Medical College and Hospital, Ludhiana were initially screened for the study. Initially 84 patients with T score < -1SD on DEXA scan, meeting inclusion criteria were enrolled for study. Two patients withdrew their consent after 1 month and two patients one each in case and control group died within first two months. So a total of 80 patients finally

completed the study period duration and were included for final analysis. Patients were randomized into two equal groups as case or control by method of simple randomization using random number generator. Patients in case group were given 35 mg of alendronate once weekly i.e. 70 mg half tablet with glass of water on empty stomach in morning and were advised not to lie down for an hour after drug intake. A reduced dose of alendronate was selected 35 mg/week versus 70 mg/week (a now-routine dosing regimen) in subjects with normal renal function. The lower dose of alendronate (was based on a previous study,[70] which demonstrated an improvement in BMD at 6 months in older women with osteoporosis and normal renal function after 6 weeks of daily alendronate. A higher dose of alendronate might have affected a greater clinical change, but we elected to administer a less intense and presumably safer dosing regimen. Alendronate is cleared exclusively by the kidney through glomerular filtration and active tubular secretion.

Fifty three patients had evidence of osteopenia i.e. T score <- 1SD on DEXA scan. Twenty seven patients had evidence had evidence of osteoporosis i.e. T score < - 2.5 SD on DEXA scan.

23 patients (32.5%) were female and 57 patients (67.5%) were male, thus giving a male to female ratio of 2.4:1. In a study done by Wetmore et al on 31 CKD5D patients 22 (70%) were males and nine (30%) were females.[70] This can also be explained by higher male to female ratio seen normally in hemodialysis population.

57(67.5%) of patients were in age group older than 50. Only 10 (12.5%) were younger than age of 40. Mean age of control and case group was 54.86 (SD=13.13) and 53.57 (SD=12.39) respectively for CKD 3 group. Mean age of control and case group was48.33 (SD=11.00) and 58.67 (SD=5.16) respectively for CKD 4 group. Mean age of control and case group was 60.00 (SD=7.85) and 50.71 (SD=14.63) respectively for CKD 5 group. Mean age of control and case group was 56.15 (SD=11.23) and 57.80 (SD=7.68) respectively for CKD 5D group. In a study done by Wetmore et al mean age was 59 (SD=11) for case and 58 (SD=12) for control group respectively.

A total of 14 (17.5%), 12 (15%), and 14 (17.5%) were in CKD stage 3, 4 and 5 respectively. 40 (50%) patients had CKD 5D stage. This was in contrast to other studies where CKD 5D were not included in same study. In most of studies CKD patients were not directly included in study as these were done on general population and during their final analysis they further analyzed the data for CKD patients.

The study by Miller et al [17] was based on an analysis of data from nine placebo controlled clinical trials of risedronate in 8996 osteoporotic women. In this combined data from nine randomized, double-blind, placebo-controlled phase III risedronate trials were analyzed. Of the 9883 patients evaluated in the primary intent-to-treat analysis, 8996 (91%) had some degree of renal impairment. Renal impairment was classified as severe in 572 (7%), moderate in 4071 (45%), and mild in 4353 (48%). There was no CKD 5D patient.

Jamal et al [52] used data from 6458 subjects from the Fracture Intervention Trial. This was a placebo controlled randomized clinical trial of alendronate in post-menopausal women. The renal function was estimated, using Cockcroft Gault, for these subjects allowing them to be categorized as having severely reduced renal function (CrCl <45mL/min) or moderately reduced or normal renal function (>45mL/min). Of the 6458 women that were studied, 581 women (9.9%) had an eGFR of <45 ml/minute, and 2409 (37.3%) had an eGFR between 45 and 59 ml/minute. In this trial, the upper limit of serum creatinine was 144 µM about one half of the women had stage 2 CKD, 45% had stage 3 CKD, but <20 women had stage 4 CKD.

Furthermore, women were excluded from the osteoporosis trial if they had evidence of increased serum PTH levels or alkaline phosphatase activity, which are frequently manifestations of the bone disease seen in stage 4 CKD. Therefore, the results of their study did not show any difference in safety or efficacy in patients with or without renal dysfunction. But in this study most of patients had mild- moderate renal dysfunction. In contrast our study also had CKD 3-5D patients.

Jamal et al [98] evaluated the effects of Denosumab on fracture and BMD by level of kidney function in postmenopausal women included in

FREEDOM study. By the CG, 73 women had stage 4 CKD; 2817 had stage 3, 4069 had stage 2 CKD, and the remaining 842 women had stage 1 CKD. By the MDRD, 17 women had stage 4 CKD, 1078 stage 3 CKD, 5413 had stage 2 CKD, and the remaining 1298 women had stage 1 CKD. None of these subjects had stage 5 CKD.

Mean SBP for control and case group was 128.85 (SD= 6.45) and 129.30 (SD= 9.56) respectively. Mean DBP for control and case group was 81.70 (SD= 4.85) and 81.45 SD= 5.14) respectively.

Five patients in control and six patients in case group had underlying LV dysfunction. The two patients in control and three in case group had LVEF between 30-40%.

Baseline mean creatinine was 3.99(SD= 1.24) and 4.15(SD= 1.32) for control and case group respectively.

When all patients irrespective of CKD stage were compared, mean creatinine values were 3.99(SD=1.24), 4.47(SD=1.41), 4.60(SD=1.46) and 4.65 (1.45) at baseline, 3 months, 6months and 12 months respectively in control group. Mean creatinine values were 4.15 (SD=1.32), 4.28(SD=1.53), 4.36(SD=1.48) and 4.72 (1.56) at baseline, 3 months, 6months and 12 months respectively in case group. There was no significant change in mean creatinine at follow up between case and control group.

Baseline mean creatinine was 2.29(SD= 0.63) and 1.99(SD= 0.41) for control and case group respectively for CKD 3 subgroup. Mean creatinine values were 2.29(SD=0.63), 2.31(SD=0.76), 2.59(SD=1.03) and 2.94 (1.42) at baseline, 3 months, 6months and 12 months respectively in control group. Mean creatinine values were 1.99 (SD=0.41), 2.03(SD=0.35), 2.16(SD=0.34) and 2.31 (0.38) at baseline, 3 months, 6months and 12 months respectively in case group. There was statistically no difference in change in the mean value of creatinine at 3, 6 and 12 months between control and case group. This was -0.27, -0.63, -0.36 at 3, 6 and 12 months for controls. This was -0.13, -0.29, -0.16 at 3, 6 and 12 months for cases. At the end of one year two patient each from case and control group progressed to CKD4 stage. This may be due to progression of the disease rather than adverse

effect of the drug because equal no patients from both the group had progression of the disease.

Baseline mean creatinine was 4.08 (SD= 0.56) and 4.20 (SD= 1.01) for control and case group respectively CKD 4 subgroup. Mean creatinine values were 4.08 (SD=0.56), 5.30 (SD=1.36), 5.68 (SD=1.31) and 5.23 (1.35) at baseline, 3 months, 6months and 12 months respectively in control group. Mean creatinine values were 4.20 (SD=1.01), 4.93 (SD=1.42), 4.53 (SD=1.02) and 4.95 (0.98) at baseline, 3 months, 6 months and 12 months respectively in case group.

There was statistically no difference in change in the mean value of creatinine at 3, 6 and 12 months between control and case group. This was -0.38, 0.07 and 0.45 at 3, 6 and 12 months for controls. This was 0.40, -0.02, -0.42 at 3, 6 and 12 months for cases. At the end of one year two patient each from case and control group progressed to CKD5 stage. This may be due to progression of the disease rather than adverse effect of the drug because equal no patients from both the group had progression of the disease.

Baseline mean creatinine was 4.67 (SD= 1.11) and 5.06 (SD= 0.97) for control and case group respectively CKD 5 subgroup. Mean creatinine values were 4.67 (SD=1.11), 4.97 (SD=0.86), 5.54 (SD=0.99) and 6.07 (0.73) at baseline, 3 months, 6months and 12 months respectively in control group. Mean creatinine values were 5.06 (SD=0.97), 5.54 (SD=0.99), 5.139 (SD=1.30) and 6.20 (0.97) at baseline, 3 months, 6months and 12 months respectively in case group.

There was statistically no difference in change in the mean value of creatinine at 3, 6 and 12 months between control and case group. This was 0.30, 0.24, -0.06 at 3, 6 and 12 months for controls. This was -0.29, -0.55, -0.26 at 3, 6 and 12 months for cases.

In our study eGFR was calculated using CKD-EPI equation compared to other studies where Cockcroft and MDRD equation were used.[6,17] There was statistically no significant difference in mean e GFR between two groups with CKD stage 3-5 at the end of the study. Equal number of patients i.e. two from both case and control group progressed from CKD stage 3 to 4 and CKD stage 4 to 5.

There was no significant increase in proteinuria for various CKD stages anytime during study period in any patient in both case or control groups.

In study done by Miller et al [17], was based on an analysis of data from nine placebo controlled clinical trials of risedronate in 8996 osteoporotic women. Renal impairment was classified as severe in 572 (7%), moderate in 4071 (45%), and mild in 4353 (48%). Within each renal impairment subgroup, the two treatment groups (placebo and risedronate 5 mg) were very similar with respect to baseline demographic and disease characteristics. Similar percentages of patients in the two treatment groups were categorized as having severe, moderate, or mild renal impairment. In both treatment groups, the patients with the most severe renal impairment were older, frailer, and had more severe osteoporosis. At baseline, the overall median (interquartile range) creatinine clearance was 49.5 (40.0–59.6) ml/min (range, 14.1–79.9 ml/min) for the placebo group and 49.2 (39.7–59.5) ml/min (range, 13.2–79.9 ml/min) for the risedronate 5 mg group. The incidence of overall adverse effects was similar within and between treatment groups in the subgroups of patients with severe, moderate, or mild renal impairment. Statistically and clinically, there were no significant differences. The most common urinary- and renal function–related adverse event was urinary tract infection, which was noted in 10–13% in each treatment group in each renal impairment subgroup. The differences between the placebo and risedronate 5 mg groups in the changes from baseline in serum creatinine at 6, 12, or 24 months or at the endpoint were not significant in any of the renal impairment subgroups.

Jamal et al [52] used data from 6458 subjects from the Fracture Intervention Trial. This was a placebo controlled randomized clinical trial of alendronate in post-menopausal women. Of the 6458 women that were studied, 581 women (9.9%) had an eGFR of <45 ml/minute, and 2409 (37.3%) had an eGFR between 45 and 59 ml/minute. There was a small significant increase in serum creatinine from baseline to the 3-year follow-up (mean at baseline: 1.05 ± 0.16 versus mean at

follow-up: 1.06 ± 0.16; p < 0.00001), but the increase in serum creatinine over the study period was the same in those with and without reduced renal function (mean increase in both groups: 0.01 ± 0.10;p=0.88) and was the same in both the placebo- and alendronate-treated groups (mean increase: 0.01 ± 0.10; p=0.99).

Boonenet al [93] evaluated patients with GFR < 35 mL/min/1.73 m2 receiving zoledronic acid and did not describe worsening of renal function. In contrast, nephrotoxicity in patients receiving pamidronate or ibandronate were reported in a review. Intravenous bisphosphonates reduce fracture risk but have been associated in rare cases with deteriorating renal-function in cancer patients. The renal effects of zoledronic acid were assessed in osteoporotic postmenopausal women from 27 countries who received three annual infusions of zoledronic acid or a placebo in a randomized, double-blind trial. Serum creatinine, estimated creatinine clearance and urinary protein were measured before and after at least one infusion in a predefined renal safety cohort of 5035 equally divided patients. This group was compared to 7714 patients whose parameters were measured annually. Significantly more transient pre- to post-infusion increases in serum creatinine occurred in zoledronic acid than placebo-treated patients with significant elevations, relative to pre-infusion, only in the second year. All 31 zoledronic acid and 8 of 10 patients on placebo recovered their pre-infusion serum creatinine value within 12 months. No differences in mean changes in serum creatinine, estimated creatinine clearance or adverse renal events were found. The study found that transient changes in renal function can occur following an annual zoledronic acid infusion but, in the In another double-blind, placebo-controlled trial by Black et al, 3889 patients (mean age, 73 years) were randomly assigned to receive a single 15-minute infusion of zoledronic acid (5 mg) and 3876 were assigned to receive placebo at baseline, at 12 months, and at 24 months; the patients were followed until 36 months. Long term, renal function was not different from control patients. Adverse events, including change in renal function, were similar in the two study groups.

Miller et al [96] have recently published a review of the literature on the renal safety of bisphosphonate use for osteoporosis. The authors concluded that the benefits outweigh risks; and even in elderly, frail, osteoporotic patients with renal impairment, intravenous bisphosphonate therapy administration in accordance with the prescribing information did not result in long term renal function decline.

There was no difference in mean ALP level at baseline, 3, 6 and 12 months between control and case group. This was 150.10, 145.33, 148.00, 145.40 at baseline, 3, 6 and 12 months for controls. This was 146.45, 149.93, 148.50, 141.63 at baseline, 3, 6 and 12 months for cases.

There was no difference in mean ALP level at baseline, 3, 6 and 12 months between controls and cases group of CKD3 subgroup. This was 144.14, 144.57, 148.71, 141.71 at baseline, 3, 6 and 12 months for controls. This was 148.57, 145.57, 156.57, 151.29 at baseline, 3, 6 and 12 months for cases.

There was no difference in mean ALP level at baseline, 3, 6 and 12 months between controls and cases group of CKD4 subgroup. This was 153.83, 147.33, 15.67, 149.50 at baseline, 3, 6 and 12 months for controls. This was 146.17, 148.83, 151.67, 138.83 at baseline, 3, 6 and 12 months for cases.

There was no difference in mean ALP level at baseline, 3, 6 and 12 months between controls and cases group of CKD5 subgroup. This was 155.71, 140.43, 143.57, 141.57 at baseline, 3, 6 and 12 months for controls. This was 146.71, 150.43, 144.14, 148.00 at baseline, 3, 6 and 12 months for cases.

There was no difference in mean ALP level at baseline, 3, and 6 months between controls and cases group of CKD5D subgroup. But difference was significant at 12 months. The mean ALP was 149.10, 146.70, 148.20, 146.80 at baseline, 3, 6 and 12 months for controls. This was 145.70, 151.75, 146.25, 136.85 at baseline, 3, 6 and 12 months for cases.

In a study done by Wetmore et al [70] in 31 patients of CKD5D the base line ALP (mkat/L) was 1.6 ± 0.6 (95 ± 36 IU/L) in alendronate group and 1.5 ± 0.5 (85 ± 31 IU/L) placebo group. This was 1.8 ± 0.5 (104 ± 30 IU/L) in alendronate group and 1.6 ± 0.7 (92 ± 38 IU/L) in placebo group after 6 months of alendronate therapy. There was no statistically significant difference between 2 groups.

Difference in ALP at 12 month in our study compared to this study was due prolonged duration of treatment in our study.

Bone specific alkaline phosphatase could not be done in our study because of non-availability. Improvement in BMD would also correlate the improvement in levels of bone specific alkaline phosphatase.

Patients with low PTH levels, who would be more likely to have low bone turnover disease were not included. Similarly, patients with extremely high PTH and who would be more likely to have hyperparathyroid bone disease were not studied. A theoretical concern about bisphosphonate toxicity in CKD patients relates to the low bone turnover that is a direct effect of the drugs.

There was no difference in mean PTH level at baseline, 3 and 6 months between control and case group. PTH values were 194.95, 194.03, 194.13, at baseline, 3, 6 and 12 months for controls. These were 197.30, 196.18, 194.93, at baseline, 3, and 6 months for cases. But there was statistically significance difference in mean PTH level between control and cases at 12 month (P=0.047). There was statistically no difference in change in the mean value of PTH at 3, and 6 months between control and case group. But difference was significant at 12 months (P =0.04)

There was statistically no significant difference in mean PTH level at baseline, 3, 6 and 12 months between control and case groups of CKD3. PTH values were 193.00, 190.00, 194.14, 186.43, at baseline, 3, 6 and 12 months for controls. These were 199.71, 198.71, 194.86, 182.29 at baseline, 3, 6 and 12 months for cases. There was also statistically no significant difference in change in mean PTH level at 6 and 12 months between control and cases. Similar results were seen in study done by Ishani et al.[103]

There was no difference in mean PTH level at baseline, 3, 6 and 12 months between control and case groups of CKD4. PTH values were 193.50, 190.67, 183.83, 183.50, at baseline, 3, 6 and 12 months for controls. These were 195.17, 191.33, 195.83, 174.67 at baseline, 3,6 and 12 months for cases. But there was statistically significance difference in change mean PTH level between control and cases at 6 and 12 months.

There was no difference in mean PTH level at baseline, 3, 6 and 12 months between control and case group of CKD5. PTH values were 196.57, 195.57, 191.14, 184.86, at baseline, 3, 6 and 12 months for controls. These were 201.43, 200.71, 192.43, 180.43 at baseline, 3,6 and 12 months for cases. But there was also statistically no significance difference of change in mean PTH level between control and cases.

There was statistically no difference in mean PTH level at baseline, 3, 6 and 12 months between control and case group of CKD 5D. PTH values were 195.50, 195.55, 198.25, 193.55, at baseline, 3, 6 and 12 months for controls. These were 195.65, 195.15, 195.55, 187.35 at baseline, 3, 6 and 12 months for cases. Also there was statistically no significance difference of change in mean PTH level between control and cases at 6 and 12 months.

In a study done by Wetmore et al [70] in 31 patients of CKD5D the baseline mean PTH was 20.9± 10.0 (198 ± 95 ng/mL) in alendronate group and 16.4 ±8.1 (156 ±77 ng/mL) in placebo group. This was 27.5 ± 14.9 (261 ± 141 pg/mL) in alendronate group and 25.4 ± 27.1 (241 ± 257 pg/mL) in placebo group after 6 months of alendronate therapy. There was no statistically significant difference between two groups. The results were similar to our study.

In a study done by Chen et al [100] after treating with Dmab in the first month, most patients had increased iPTH levels, which dramatically decreased from 1702.1±181.9 to 518.8± 126.8 pg/mL by the end of the study. So at the end the results were similar to our study.

There was improvement in mean T score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. But this change in mean T score was statistically significant between two groups at 6 and 12 month.

Mean Z score at level of lumbar spine also shown improvement at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of Z score was statistically significant between 2 groups at 6 and 12 month.

Mean lumbar spine BMD was 1.05 for case and 1.13 for control respectively at baseline. It was 1.14 and 1.09 for case and control respectively at 6 months. It was 1.25 and 1.02 for case and control respectively at 12 month.

There was improvement in mean BMD at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

There was improvement in mean T score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This improvement in mean T score was statistically significant between 2 groups at 6 and 12 month.

Mean Z score at level of femur neck also shown improvement at 6 and 12 months in patients, who received oral alendronate compared to controls. This improvement in mean T score was statistically significant between 2 groups at 6 and 12 month.

Mean femur neck BMD was 0.83 for case and 0.90 for control respectively at baseline. It was 0.91and 0.84 for case and control respectively at 6 months. It was 1.06 and 0.79 for case and control respectively at 12 month.

There was improvement in mean BMD at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

There was improvement in mean T score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement mean T score was statistically significant between 2 groups at 6 and 12 month.

Mean Z score of total hip also shown improvement at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement mean Z score was statistically significant between 2 groups at 6 month.

Mean total hip BMD was 0.85 for case and 0.96 for control respectively at baseline. It was 0.96and 0.89 for case and control respectively at 6 months. It was 1.09 and 0.84 for case and control respectively at 12 month.

There was improvement in mean BMD at level of total hip at 6 and 12 month in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

Jamal et al from FIT trail [52] found that compared with placebo-treated women, alendronate increased total hip BMD by 4.9 ± 8.7% over a mean follow-up of 3 years. Women with a reduced eGFR had a 5.6% (95% CI: 4.8–6.5) increase in total hip BMD compared with 4.8% (95% CI: 4.6–5.0) among women with normal to moderate renal dysfunction (interaction: p= 0.04). Compared with placebo, alendronate increased spine BMD by 6.6 ± 5.8%, but in contrast to effects on hip BMD, there was no significant interaction between renal function and the increase in BMD (interaction: p =0.75). Similarly in our study there was no significant interaction between renal function and the increase in BMD. Similarly, there was no significant interaction between renal function and the increase in femoral neck (p= 0.32). Among women with osteoporosis, the annualized percent changes in total hip, femoral neck, and spine BMD were similar among those with a CrCl <45 ml/minute and those with CrCl ≥45 ml/minute, with no evidence of an interaction between renal function and treatment assignment. Similar results were seen in our study.

Chen et al [100] observed similar results with denosumab. This 6-month prospective, open-labeled study evaluated 12 patients (five women, seven men; mean age 53.5±3.8 y). All had intact PTH (iPTH>1000 pg/mL), low bone mass (T-score<1.0 SD), and bone pain. The BMD was significantly improved at the end of the study period, with mean increase in femoral neck BMD of 23.7% ± 4.0% from the initial 0.57 ± 0.04 g/cm2 to 0.72 ± 0.05 g/cm2 and mean increase in lumbar spine BMD of 17.1%± 2.6% from the initial 0.81± 0.04 g/cm2 to 0.94±0.05 g/cm2. The counterpart results of the control group revealed no significant changes in femoral neck BMD with the initial 0.61 ± 0.04 g/cm2 to 0.63 ± 0.04 g/cm2. Similar results were seen in our study.

Combined data from nine randomized, double-blind, placebo-controlled phase III

risedronate trials were analyzed by Miller et al.[17] The patients in these studies had no markedly abnormal laboratory parameters that were considered clinically significant and no evidence of significant disease. This analysis included patients who received placebo (*n* = 4500) or risedronate 5 mg (*n* = 4496) for up to 3 years (average duration of exposure, 2 years) and who had renal impairment (creatinine clearance [CrCl] < 80 ml/min). CrCl was estimated by the Cockcroft and Gault method, based on age, weight, and serum creatinine. Patients were categorized as having mild (CrCl ≥50 to <80 ml/min), moderate (CrCl ≥30 to <50 ml/min), or severe (CrCl < 30 ml/min) renal impairment. The mean percent increase from baseline to endpoint in BMD at the lumbar spine and femoral neck and trochanter was significantly greater in the risedronate 5 mg group than in the placebo group in all three renal impairment subgroups, except at the femoral neck in the severe renal impairment subgroup. Mean percent changes (SE) from baseline to endpoint in lumbar spine BMD were −1.37% (1.72%) in the placebo group versus +4.23% (1.82%) in the risedronate group in patients with severe renal impairment; −0.47% (0.50%) in the placebo group versus +4.33% (0.51%) in the risedronate group in patients with moderate renal impairment; and −0.14% (0.19%) in the placebo group versus

+3.96% (0.18%) in the risedronate group in patients with mild renal impairment (p < 0.001 for all comparisons). The increases from baseline in BMD were greater in the risedronate 5 mg group than in the placebo group at all three skeletal sites at 6, 12, and 24 months in each renal impairment subgroup. The results were similar to our study.

FOR CKD3

There was improvement in mean T score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. But this improvement in mean of T score was statistically significant between 2 groups at 6 and 12 month.

Mean Z score at level of lumbar spine shown improvement at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of Z score was statistically significant between 2 groups at 6 and 12 month.

Mean lumbar spine BMD was 1.02 for case and 1.11 for control respectively at baseline. It was 1.17 and 1.08 for case and control respectively at 6 months. It was 1.30 and 1.01 for case and control respectively at 12 month.

There was improvement in mean BMD at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

There was improvement in mean T score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This improvement in mean T score was statistically significant between 2 groups at 6 and 12 month.

Mean Z score at level of femur neck shown improvement at 6 and 12 months in patients, who received oral alendronate compared to controls. This improvement in mean T score was statistically significant between 2 groups at 6 and 12 month.

Mean femur neck BMD was 0.93 for case and 1.10 for control respectively at baseline. It was 1.00 and 1.01 for case and control

respectively at 6 months. It was 1.37 and 0.95 for case and control respectively at 12 month.

There was improvement in mean BMD at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

There was improvement in mean T score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement mean T score was statistically significant between 2 groups at 6 and 12 month.

Mean Z score of total hip shown improvement at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement mean Z score was statistically significant between 2 groups at 6 month.

Mean total hip BMD was 0.22 for case and 1.13 for control respectively at baseline. It was 1.18 and 1.05 for case and control respectively at 6 months. It was 1.32 and 0.98 for case and control respectively at 12 month.

There was improvement in mean BMD at level of total hip at 6 and 12 month in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in improvement was statistically significant between 2 groups at 6 and 12 month. Similar results were seen in other studies.[17,52,100]

FOR CKD4

There was improvement in mean T score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. But this improvement in mean of T score was statistically significant between 2 groups at 6 and 12 month.

Mean Z score shown improvement at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of Z score was statistically significant between 2 groups at 6 and 12 month.

Mean lumbar spine BMD was 1.02 for case and 1.28 for control respectively at baseline. It was 1.07 and 1.24 for case and control respectively at 6 months. It was 1.15 and 1.16 for case and control respectively at 12 month.

There was improvement in mean BMD at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

There was improvement in mean T score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This improvement in mean T score was statistically significant between 2 groups at 12 month.

There was improvement in mean Z score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This improvement in mean T score was statistically significant between 2 groups at 6 and 12 month.

Mean femur neck BMD was 0.79 for case and 0.91 for control respectively at baseline. It was 0.84 and 0.83 for case and control respectively at 6 months. It was 0.97 and 0.78 for case and control respectively at 12 month.

There was improvement in mean BMD at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in mean BMD between two groups was statistically significant at 12 month. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

There was improvement in mean T score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement mean T score was statistically significant between 2 groups at 6 and 12 month.

Mean Z score of total hip shown improvement at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement mean Z score was statistically significant between 2 groups at 6 and 12 month.

Mean total hip BMD was 0.87 for case and 1.04 for control respectively at baseline. It was 0.96 and 0.99 for case and control respectively at 6 months. It was 1.09 and 0.96 for case and control respectively at 12 month.

There was improvement in mean BMD at level of total hip at 6 and 12 month in patients, who received oral alendronate compared to controls. This difference in improvement was statistically significant between 2 groups at 6 and 12 month. Similar results were seen in other studies.[17, 52,100]

There was no relationship between level of renal function and improvement in DEXA finding.

FOR CKD5

There was improvement in mean T score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This improvement in mean of T score was statistically significant between 2 groups at 6 and 12 month.

Mean Z score at level of lumbar spine shown improvement at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of Z score was statistically significant between 2 groups at 6 and 12 month.

Mean lumbar spine BMD was 1.02 for case and 1.16 for control respectively at baseline. It was 1.10 and 1.14for case and control respectively at 6 months. It was 1.26 and 1.08 for case and control respectively at 12 month.

There was improvement in mean BMD at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

There was improvement in mean T score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This improvement in mean T score was statistically significant between 2 groups at 12 month.

Mean Z score at level of femur neck shown improvement at 6 and 12 months in patients, who received oral alendronate compared to

controls. This improvement in mean T score was statistically significant between 2 groups at 6 and 12 month.

Mean femur neck BMD was 0.81 for case and 0.81 for control respectively at baseline. It was 0.94 and 0.78 for case and control respectively at 6 months. It was 1.04 and 0.77 for case and control respectively at 12 month.

There was improvement in mean BMD at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

There was improvement in mean T score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement mean T score was statistically significant between 2 groups at 6 and 12 month.

Mean Z score of total hip shown improvement at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement mean Z score was statistically significant between 2 groups at 6 and 12 month.

Mean total hip BMD was 0.81 for case and 0.89 for control respectively at baseline. It was 0.94 and 0.86 for case and control respectively at 6 months. It was 1.03 and 0.84 for case and control respectively at 12 month.

There was improvement in mean BMD at level of total hip at 6 and 12 month in patients, who received oral alendronate compared to controls. This difference in improvement was statistically significant between 2 groups at 6 and 12 month. Similar results were seen in other studies.[17, 52,100]

FOR CKD5D

Mean lumbar spine T score was -1.38 for case and -1.86 for control respectively at baseline. It was -1.25 and -2.02 for case and control respectively at 6 months. It was -1.07 and -2.14 for case and control respectively at 12 months. There was improvement in mean T score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This improvement in mean of T

score was statistically significant between two groups at 6 and 12 month.

In a study done by Wetmore et al in 31 patients of CKD5D lumbar spine mean T-score was -0.2 ± 1.8 at baseline and -0.4 ± 1.8 at 6 months in patients who received alendronate. This was 1.3 ± 0.2 at baseline and 1.3 ± 0.2 at 6 months in patients who did not receive alendronate. There was no significant difference between the value of the mean T score between two groups. The improvement in our study compared to this study may be due to prolonged duration of treatment in our study.

Mean lumbar spine Z score was -0.51for case and -0.64 for control respectively at baseline. It was -0.39 and -0.72 for case and control respectively at 6 months. It was -0.20 and -0.78 for case and control respectively at 12 months.

There was improvement in mean Z score at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of Z score was statistically significant between 2 groups at 6 and 12 month.

In a study by Wetmore et al in patients of CKD5D lumbar spine mean Z-score was0.1 ± 1.6 at baseline and 0.0 ± 1.6 at 6 months in patients who received alendronate. This was 0.8 ± 1.9 at baseline and 0.9 ± 2.0 at 6 months in patients who did not receive alendronate. There was no significant difference between the value of the mean Z score between two groups. The improvement in our study compared to this study may be due to prolonged duration of treatment in our study.

Mean lumbar spine BMD was 1.08 for case and 1.09 for control respectively at baseline. It was 1.17 and 1.04 for case and control respectively at 6 months. It was 1.26 and 0.96 for case and control respectively at 12 month.

There was improvement in mean BMD at level of lumbar spine at 6 and 12 months in patients, who received oral alendronate compared to controls. The difference in BMD at 12 month was statistically significant between two groups. This difference in improvement was statistically significant between two groups at 6 and 12 month.

In the study by Wetmore et al lumbar spine mean BMD was 1.171 ± 0.219 at baseline and -0.007 ± 0.044 at 6 months in patients who received alendronate. This was 1.304 ± 0.204 at baseline and 0.009 ± 0.040 at 6 months in patients who did not receive alendronate. There was statistically no significant difference between the value of the mean BMD between two groups at 6 months. The improvement in our study compared to this study may be due to prolonged duration of treatment in our study.

Mean femur neck T score was -2.19 for case and -2.12 for control respectively at baseline. It was -1.99 and -2.21 for case and control respectively at 6 months. It was -1.79 and -2.36 for case and control respectively at 12 month.

There was improvement in mean T score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This improvement in mean T score was statistically significant between 2 groups at 12 month.

In the study by Wetmore et al femur neck mean T score was -1.8 ± 1.2 at baseline and -1.8 ± 1.2 at 6 months in patients who received alendronate. This was -1.1 ± 1.2 at baseline and -1.3 ± 1.2 at 6 months in patients who did not receive alendronate. There was statistically significant difference between the value of the mean T score between two groups at 6 months.

Mean femur neck Z score was -0.49 for case and -0.63 for control respectively at baseline. It was -0.40 and -0.69 for case and control respectively at 6 months. It was -0.27 and -0.79 for case and control respectively at 12 months.

There was improvement in mean Z score at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This improvement in mean T score was statistically significant between 2 groups at 6 and 12 month.

In the study by Wetmore et al femur neck mean Z score was -1.2 ± 1.2 at baseline and --1.2 ± 1.2 at 6 months in patients who received alendronate. This was-0.7 ± 0.8 at baseline and -0.8 ± 0.8 at 6 months in patients who did not receive alendronate. There was statistically

significant difference between the value of the mean Z score between two groups at 6 months.

Mean femur neck BMD was 0.82 for case and 0.86 for control respectively at baseline. It was 0.89 and 0.81 for case and control respectively at 6 months. It was 0.99 and 0.75 for case and control respectively at 12 month.

There was improvement in mean BMD at level of femur neck at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement was statistically significant between two groups at 6 and 12 month.

In the study by Wetmore et al femur neck mean BMD was 0.804 ± 0.157 at baseline and -0.001 ± 0.044 at 6 months in patients who received alendronate. This was 0.912 ± 0.168 at baseline and -0.021 ± 0.038 at 6 months in patients who did not receive alendronate. There was statistically no significant difference between the value of the mean BMD of femur neck between two groups at 6 months. The improvement in our study compared to this study may be due to prolonged duration of treatment in our study.

Mean total hip T score was -2.10 for case and -1.81 for control respectively at baseline. It was -1.91 and -1.94 for case and control respectively at 6 months. It was -1.75 and -2.09 for case and control respectively at 12 month.

There was improvement in mean T score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement mean T score was statistically significant between 2 groups at 6 and 12 month.

In the study by Wetmore et al [70] total hip T score was -1.8 ± 1.3 at baseline and -1.8 ± 1.2 at 6 months in patients who received alendronate. This was -0.9 ± 1.2 at baseline and -1.0 ± 1.2 at 6 months in patients who did not receive alendronate. There was statistically no significant difference between the value of the mean T score between two groups at 6 months. The improvement in our study compared to this study may be due to prolonged duration of treatment in our study.

Mean total hip Z score was -1.19 for case and -0.58 for control respectively at baseline. It was -0.91 and -0.68 for case and control respectively at 6 months. It was -0.02 and -0.50 for case and control respectively at 12 months.

There was improvement in mean Z score of total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This difference in improvement mean Z score was statistically significant between 2 groups at 6 month.

In the study by Wetmore et al [70] total hip Z score was -1.4 ± 1.4 at baseline and --1.4 ± 1.3 at 6 months in patients who received alendronate. This was 0.7 ± 1.0 at baseline and -0.8 ± 1.0 at 6 months in patients who did not receive alendronate. There was statistically no significant difference between the value of the mean Z score between two groups at 6 months. The improvement in our study compared to this study may be due to prolonged duration of treatment in our study.

Mean total hip BMD was 0.80 for case and 0.91 for control respectively at baseline. It was 0.90 and 0.82 for case and control respectively at 6 months. It was 1.03 and 0.76 for case and control respectively at 12 month. The difference in BMD between two groups was statistically significant.

There was improvement in mean BMD at level of total hip at 6 and 12 month in patients, who received oral alendronate compared to controls. This difference in improvement was statistically significant between 2 groups at 6 and 12 month.

In the study by Wetmore et al [70] total hip mean BMD was 0.830 ± 0.176 at baseline and -0.001 ± 0.041at 6 months in patients who received alendronate. This was 0.956 ± 0.162 at baseline and -0.011 ± 0.030 at 6 months in patients who did not receive alendronate. There was statistically no significant difference between the value of the mean BMD of femur neck between two groups at 6 months. The improvement in our study compared to this study may be due to prolonged duration of treatment in our study.

Significant improvement in T score, Z score and BMD at all sites i.e. lumbar spine, femur neck and total hip in CKD 5D patients in our study

compared to study done by Wetmore is explained by longer duration of treatment for one year in our study.

There was no difference in outcome of alendronate therapy in terms of efficacy i.e. improvement in DEXA finding and incidence of adverse effects between diabetic and non-diabetic CKD patients.

Two patients in control group and one in case group had fracture. Only 2 patients (CKD5D) who received oral alendronate had evidence abdominal aorta calcification on lateral X ray of lumbar spine compared to 5 patients (CKD5D=4, CKD5=1), who did not receive alendronate. Vascular calcifications are a serious problem in patients with CKD – mineral and bone disorder (CKD-MBD). The interactions between bisphosphonates and vascular calcifications are complex and are not well understood. Etidronate inhibits mineralization and has been shown to improve vascular calcifications in some animal models and small patient studies. This inhibition is dose-dependent and is not seen with the vastly smaller doses used with the newer generation of amino-bisphosphonates. Studies in subjects with osteoporosis as well as those with late stages of CKD have not shown any significant difference in the extent of calcifications comparing alendronate oribandronate with placebo.

Only 2 patients (CKD5D) who received oral alendronate had evidence of sub periosteal resorbtion of phalanges on X ray hand compared to 4 patients (CKD5D=3, CKD5=1), who did not receive alendronate.

Compared with placebo-treated women, alendronate reduced the risk of clinical fractures (OR =0.8; 95% CI: 0.70–0.9) regardless of renal function in FIT. Furthermore, treatment with alendronate reduced the risk of clinical fractures to a similar degree in those with (OR: 0.78; 95% CI: 0.51–1.21) and without reduced renal function (OR: 0.80; 95% CI: 0.70–0.93; *p* for interaction=0.89). There were 119 morphometric spine fractures over a maximum period of 4 years of follow-up (3 years in the vertebral fracture arm and 4 years in the clinical fracture arm). Overall, compared with placebo-treated women, alendronate reduced the risk of spine fractures (OR: 0.54; 95% CI: 0.37–0.78). Treatment with alendronate reduced the risk of morphometric spine fractures to a

similar degree in those with (OR: 0.72; 95% CI: 0.31–1.7) and without reduced renal function (OR: 0.50; 95% CI: 0.32–0.76; *p* for interaction=0.44).

In a study by MC clung et al [24] Overall, the incidence of hip fracture among all the women assigned to risedronate was 2.8 percent, as compared with 3.9 percent among those assigned to placebo (relative risk, 0.7; 95 percent confidence interval, 0.6 to 0.9; P=0.02). In the group of women with osteoporosis (those 70 to 79 years old), the incidence of hip fracture among those assigned to risedronate was 1.9 percent, as compared with 3.2 percent among those assigned to placebo (relative risk, 0.6; 95 percent confidence interval, 0.4 to 0.9; P=0.009). In the group of women selected primarily on the basis of nonskeletal risk factors (those at least 80 years of age), the incidence of hip fracture was 4.2 percent among those assigned to risedronate and 5.1 percent among those assigned to placebo (P=0.35).

This results were different from our study, where overall incidence of fractures was less in both case and control group. Two patients in control group and one in case group had fracture on x ray of DL spine.

Five patients had initially GI intolerance to alendronate, one had osteonecrosis of jaw, one had dermatological reaction to alendronate, but none of them required stoppage of drug due to side effects. Similar results were found in other studies. Total three patients died after 12 months two in control and one alendronate group. All three had underlying cardiac illness and none of death was related to known side effects of treatment.

Similar results were seen in study by Wetmore et al [70] in CKD 5D patients, three subjects experienced gastric discomfort after the first dose, but tolerated subsequent doses without side effects. No patient had to be discontinued from the alendronate.

In study by Miller et al the incidence of overall, urinary- and renal function–related, and specific renal function–related adverse events was similar within and between treatment groups in the subgroups of patients with severe, moderate, or mild renal impairment. Statistically and clinically, there were no significant differences between two groups

with or without risedronate. The most common urinary- and renal function–related adverse event was urinary tract infection, which was noted in 10–13% in each treatment group in each renal impairment subgroup.

Adverse events were assessed in FIT by Jamal et al [52] every 3 months, Of the 6458 women in the study, 6426 reported an adverse event, but there was no difference in the frequency of reported events among women with reduced renal function (576 of 581 women or 99.1%) compared with women without reduced renal function (5850 of 5877 or 99.5%; *p*=0.189). More specifically, there was no difference in the frequency of gastrointestinal events (4.5% in women with reduced renal function compared with 5.2% among women without reduced renal function; *p* = 0.5), cerebrovascular events (2.2% in both groups; *p* = 0.9), cardiovascular events (2.6% in women with reduced renal function compared with 3.2; *p*= 0.4), arrhythmias (2.4% in women with reduced renal function compared with 2.1; *p*= 0.7), malignancies (4.3% in women with reduced renal function compared with 5.0 among women without reduced renal function; *p*= 0.4), and death (1.6% in women with reduced renal function compared with 1.9; *p*= 0.5).

Other adverse cardiovascular effects have not been consistently seen in patients with ordinary osteoporosis, although there have been some studies with higher incidence of atrial fibrillation. A review by the US Food and Drug Administration did not find a significant increase in arrhythmias. In the largest registration trial for alendronate, the event rates for myocardial infarction were not publicly released. A retrospective cohort study included 9604 women with stages 3 – 4 CKD who did not have a previous serious cardiovascular event. They were followed for 3.9 years to ascertain mortality and rate of serious cardiac events. In 3234 women who had been exposed to bisphosphonates, the all-cause mortality was significantly better than in the patients who had not taken bisphosphonates. However, there was no benefit for cardiovascular events. Notably, in those patients who initially had some cardiac disease, the hazard ratios were 1.20 for death and 1.24 for a serious cardiovascular end point.

Furthermore, there was no difference in the frequency of renal adverse events in women with reduced renal function (12 of 581 or 2.1%) compared with those without (137 of 5877 or 2.3%; *p*= 0.68). But in our study all patients were having CKD at baseline and patients with normal renal function were not included. There was statistically no significant difference in mean e GFR between two groups with CKD stage 3-5 at the end of the study. Equal number of patients i.e. two from both case and control group progressed from CKD stage 3 to 4 and CKD stage 4 to 5. There was no hospitalization due to AKI as an adverse effect of the therapy in any patient at any time during the study period.

There was no increase in base line proteinuria for various CKD stages between case or control group at the end of the study. On further analysis there was no increase in base line proteinuria between diabetic and non-diabetic CKD patients. Recent studies have indicated that combining proteinuria with eGFR may provide a better predictive model for progression of chronic kidney disease. However, data on proteinuria have not been included in the publications of the pivotal trials of bisphosphonates.

LIMITATIONS OF THE STUDY:

There are several limitations to the present study

1. Firstly the sample size of our study population was small. A large sample size is required to evaluate the efficacy and adverse effects the bisphosphonates.
2. Reduced dose of alendronate was selected 40 mg/week versus 70 mg/week (a now-routine dosing regimen) in subjects with normal renal function. A higher dose or longer duration of alendronate might have affected a greater clinical change, but we elected to administer a less intense and presumably safer dosing regimen.
3. The duration of study was short i.e. over one year. A study with longer duration is required to study evaluate the efficacy and adverse effects the bisphosphonates.

4 . Bone specific alkaline phosphatase could not be done in our study because of non-availability. Improvement in BMD would also correlate the improvement in levels of bone specific alkaline phosphatase.

5. There was no significant difference in the incidence of fractures between treatment and control arm. Ideally the improvement in BMD should also be reflected in terms of incidence of fractures. But sample size of our study population was small and incidence of fractures was less in both case and control group.

6. Examination of bone histology was not done included in our study. Further studies of longer duration, and including examination of bone histology, are needed to assess whether bisphosphonates can be used to preserve BMD in CKD patients.

7. Only oral form of antiresorptive therapy was used in our study. Intravenous therapy especially like denusumab, which require less frequent dose administration could have more compliance and overall may be more cost effective.

Our study is one of the few studies done in patients with ESRD which included hemodialysis patients, where efficacy and safety of antiresorptive therapy in form of oral alendronate is studied. Previous randomized trails did not include the patients with renal dysfunction. Only post hoc studies from these randomized trials on the subjects with eGFR less than 60 have shown that the fracture reduction was similar to rates in subjects with a normal eGFR. But our study included with patients with ESRD including dialysis patients. So our study demonstrated the safety of antiresorptive therapy in terms of improvement in BMD on DEXA in patients with CKD 3-5D. Oral alendronate was found to be safe in these patients without significant adverse effects compared to placebo. But a further study with larger patient number is required to study whether this improvement in BMD in DEXA is translated into outcomes in form improvement in bone histology and improvement in incidence of fractures.

SUMMARY AND CONCLUSION

This prospective case control study was conducted in the Department of Nephrology, Dayanand Medical College and Hospital Ludhiana. The study period was from Feb 2018 to July 2019.

- A total of 150 patients of CKD age 3 -5D presenting to Nephrology ward, OPD and/or dialysis unit were initially screened for the study.
- A total of 80 patients with T score < -1SD on DEXA scan, meeting inclusion criteria finally completed the study period duration and were included for final analysis.
- Fifty three patients had evidence of osteopenia i.e. T score <- 1SD on DEXA scan. Twenty seven patients had evidence had evidence of osteoporosis i.e. T score < - 2.5 SD on DEXA scan.
- Patients were randomized into two equal groups as case or control.
- Patients in case group were given 35 mg of alendronate once weekly i.e. 70 mg half tablet with glass of water on empty stomach in morning and were advised not to lie down for an hour after drug intake.
- 23 patients (32.5%) were female and 57 patients (67.5%) were male, thus giving a male to female ratio of 2.4:1.
- 57(67.5%) of patients were in age group older than 50. Only 10 (12.5%) were younger than age of 40.
- Mean age for control and case group was 54.86 (SD=13.13) and 53.57 (SD=12.39) for CKD3, 48.33 (SD=11.00) and 58.67 (SD=5.16) for CKD 4, 60.00 (SD=7.85) and 50.71 (SD=14.63) for CKD 5 group respectively.
- Mean age of control and case group was 56.15 (SD=11.23) and 57.80 (SD=7.68) respectively for CKD 5D group.
- 14 (17.5%), 12 (15%), and 14 (17.5%) were of CKD stage 3, 4 and 5 respectively. 40 (50%) patients had CKD 5D stage.
- Five patients in control and six patients in case group had underlying LV dysfunction. The two patients in control and three in case group had LVEF between 30-40%.

- Patients with adynamic bone disease (with PTH < 130 and/or bone specific alkaline phosphatase < 30) were excluded from the study.
- Baseline mean creatinine was 3.99(SD= 1.24) and 4.15(SD= 1.32) for control and case group respectively.
- There was no difference in overall mean ALP level at baseline, 3, 6 and 12 months between control and case group in CKD 3, 4 and 5. But this difference in mean ALP value was significant at 12 month for CKD 5D group.
- There was no difference in mean PTH level at baseline, 3 and 6 months between control and case group. But there was statistically significance difference in mean PTH level between control and cases at 12 month (P=0.047) when analyzed as combined irrespective of CKD stage. But this difference was not seen for individual CKD sub stage.
- Bone specific alkaline phosphatase could not be done in our study because of non-availability.
- There was improvement in mean T score at level of lumbar spine, femur neck and total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean of T score was statistically significant between two groups at 6 and 12 month irrespective of CKD stage.
- There was improvement in mean Z score at level of lumbar spine, femur neck and total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean Z score was statistically significant between two groups at 6 and 12 month irrespective of CKD stage.
- There was improvement in mean BMD at level of lumbar spine, femur neck and total hip at 6 and 12 months in patients, who received oral alendronate compared to controls. This change in mean BMD was statistically significant between two groups at 6 and 12 month irrespective of CKD stage.
- When all patients irrespective of CKD stage were compared, mean creatinine values were 3.99 (SD=1.24), 4.47 (SD=1.41), 4.60

(SD=1.46) and 4.65 (1.45) at baseline, 3 months, 6 months and 12 months respectively in control group.

- Mean creatinine values were 4.15 (SD=1.32), 4.28 (SD=1.53), 4.36 (SD=1.48) and 4.72 (1.56) at baseline, 3 months, 6 months and 12 months respectively in case group.
- Two patients from both case and control group progressed from CKD 3 to CKD 4 and similarly two patients from both case and control group progressed from CKD 4 to CKD5 at end of 12 month. None of patients progressed to CKD5D.
- There was statistically no significant difference in the change in mean creatinine at 6 and 12 month follow up between case and control group overall and for each CKD subgroup in the study.
- There was statistically no significant difference in mean eGFR between two groups with CKD stage 3-5 at the end of the study. Equal number of patients i.e. two from both case and control group progressed from CKD stage 3 to 4 and CKD stage 4 to 5.
- There was no increase in base line proteinuria for various CKD stages between case or control group at the end of the study.
- Two patients in control group and one in case group had fracture. There was no significant difference in the incidence of fractures between treatment and control arm. The overall incidence of fractures was less in our study population.
- Only two patients (CKD5D) who received oral alendronate had evidence abdominal aorta calcification on lateral X ray of lumbar spine compared to five patients (CKD5D=4, CKD5=1), who did not receive alendronate.
- Only two patients (CKD5D) who received oral alendronate had evidence of sub periosteal resorbtion of phalanges on X ray hand compared to four patients (CKD5D=3, CKD5=1), who did not receive alendronate.
- The benefit of the treatment was independent of the degree of renal impairment.

- Five patients had initially GI intolerance to alendronate, one had osteonecrosis of jaw, one had dermatological reaction to alendronate, but none of them required stoppage of drug due to side effects.
- Total three patients died after 12 months two in control and one in alendronate group. All three had underlying cardiac illness and none of death was related to side effects of treatment.
- In conclusion Low-dose alendronate, administered for longer duration, appears to be well tolerated in CKD 3-5D patients.
- The BMD, T-scores and Z score improved in treatment group compared to the placebo group over 12 months, suggesting a bone-preserving effect of alendronate.
- There are no significant renal and other adverse events. Gastrointestinal intolerance is the main adverse effect.
- So our study demonstrated the safety of antiresorptive therapy in terms of improvement in BMD on DEXA in patients with CKD 3-5D. Oral alendronate was found to be safe in these patients without significant adverse effects compared to placebo.
- But a further study with larger patient number is required to study whether this improvement in BMD in DEXA is transmitted into outcomes in form of improvement in bone histology and improvement in incidence of fractures.

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S.NO.	Name	MRD	age	Age group	sex	IPD/ OPD/ HD	Religion	address urban/rural	diagnosis	CKD stage	comorbidity cardiac	comorbidity others	CKD 5D DURATION of dialysis at timeof enrollment in months	Route Hemodialysis/ Peritoneal dialysis	Accees for HD
1	DS	39091	61	4	M	HD	sikh	urban	Diabetic Nephropathy	5D	no	no	9	HD	AV fistula
2	RS	95232	59	3	M	HD	hindu	urban	obstructive nephropathy	5D	no	hepatitis c treated, hypertension	8	HD	permanent dialysis catheter
3	NS	275234	66	4	M	HD	hindu	urban	Hypertensive Nephrosclerosis	5D	no	right solitary kidney	5	HD	AV fistula
4	SA	81489	60	3	M	HD	hindu	rural	Diabetic Nephropathy	5D	no	no	6	HD	temporary right juglar catheter
5	NS	358756	39	3	M	0PD	sikh	urban	Diabetic Nephropathy	3	no	Hypertension	0	NAD	NAD
6	HS	362450	56	3	M	HD	sikh	urban	Renal calculus disease	5D	no	Diabetes melitis 2	96	HD	AV fistula
7	NJ	146147	54	3	F	HD	sikh	urban	Hypertensive Nephrosclerosis	5D	no	no	50	HD	AV fistula
8	HS	84886	60	3	M	HD	sikh	urban	Diabetic Nephropathy	5D	no	Hypertension	72	HD	AV fistula
9	JS	372848	69	4	M	HD	hindu	urban	Hypertensive Nephrosclerosis	5D	no	Hypertension	4	HD	AV fistula
10	VA	192368	52	3	F	HD	hindu	urban	Diabetic Nephropathy	5D	no	Hypertension	38	HD	permanent dialysis catheter
11	HS	189874	60	3	M	HD	hindu	rural	Diabetic Nephropathy	5D	no	Hypertension	8	HD	AV fistula
12	RV	241271	50	2	F	HD	hindu	rural	Hypertensive Nephrosclerosis	5D	no	Hypertension	6	HD	AV fistula
13	JG	184776	55	3	M	HD	sikh	urban	Diabetic Nephropathy	5D	no	Hepatitis B positive	9	HD	AV fistula
14	RM	197400	64	4	M	HD	sikh	urban	Diabetic Nephropathy	5D	no	Hypertension	17	HD	AV fistula
15	SK	115952	59	3	M	HD	sikh	urban	Diabetic Nephropathy	5D	no	Hypertension	47	HD	AV fistula
16	SS	140578	46	2	M	HD	sikh	urban	Diabetic Nephropathy	5D	YES LVEF 40%	NO	19	HD	AV fistula
17	BK	201967	57	3	M	HD	hindu	urban	Hypertensive Nephrosclerosis	5D	no	Hypertension	32	HD	AV fistula
18	NK	43405	43	2	F	HD	hindu	urban	Hypertensive Nephrosclerosis	5D	no	Hypertension	4	HD	temporary right juglar catheter
19	GS	198374	26	1	M	HD	muslim	urban	Hypertensive Nephrosclerosis	5D	no	Hypertension	7	HD	temporary right juglar catheter
20	SK	371465	64	4	M	HD	sikh	urban	Diabetic Nephropathy	5D	no	Hypertension	6	HD	AV fistula
21	AK	132172	62	4	M	HD	sikh	urban	Diabetic Nephropathy	5D	YES LVEF 40%	no	16	HD	AV fistula
22	IS	191015	61	4	M	HD	sikh	urban	Hypertensive Nephrosclerosis	5D	no	Hypertension	21	HD	AV fistula
23	RS	451663	35	1	F	IPD	sikh	rural	Hypertensive Nephrosclerosis	4	no	Hypertension	0	NAD	NAD
24	AS	96083	46	2	M	HD	sikh	urban	CIN CKD	5D	no	no	17	HD	AV fistula
25	HK	208490	49	2	F	HD	sikh	urban	Diabetic Nephropathy	5D	no	no	13	HD	AV fistula
26	RC	23008	61	4	M	HD	hindu	urban	Diabetic Nephropathy	5D	no	no	8	HD	AV fistula
27	RS	182281	67	4	M	HD	hindu	urban	Diabetic Nephropathy	5D	no	no	7	HD	AV fistula
28	JS	151689	61	4	M	OPD	muslim	urban	Diabetic Nephropathy	4	no	no	0	NAD	NAD
29	NS	462800	64	4	M	OPD	sikh	rural	Diabetic Nephropathy	5	no	no	0	NAD	NAD
30	GS	78322	38	1	M	OPD	sikh	rural	Diabetic Nephropathy	5	no	no	0	NAD	NAD
31	SP	413783	69	4	M	HD	hindu	urban	Diabetic Nephropathy	5D	YES LVEF 32%	no	4	HD	AV fistula
32	PK	415656	54	3	F	HD	hindu	urban	Diabetic Nephropathy	5D	YES IHD	no	8	HD	AV fistula
33	BK	236044	39	1	F	OPD	hindu	urban	CIN CKD	3	no	no	0	NAD	NAD
34	TK	209973	34	3	M	IPD	hindu	rural	Diabetic Nephropathy	4	no	no	0	NAD	NAD
35	KD	402541	57	3	M	IPD	hindu	rural	Diabetic Nephropathy	5	no	no	0	NAD	NAD
36	SD	188308	61	4	M	OPD	hindu	urban	Hypertensive Nephrosclerosis	3	no	no	0	NAD	NAD
37	GK	284262	43	2	M	HD	hindu	urban	Diabetic Nephropathy	5D	no	no	3	HD	AV fistula
38	SS	135439	40	1	M	HD	sikh	urban	ADPKD	5D	no	Hypertension	13	HD	AV fistula
39	GS	184285	66	4	M	HD	sikh	urban	Diabetic Nephropathy	5D	no	Hypertension	17	HD	AV fistula
40	SA	457442	67	4	M	HD	hindu	rural	Hypertensive Nephrosclerosis	5D	YES LVEF 38%	Hypertension	15	HD	AV fistula
41	GS	330245	69	4	M	HD	hindu	rural	Diabetic Nephropathy	5D	no	Hypertension	15	HD	AV fistula
42	CK	393125	69	4	F	HD	hindu	urban	Hypertensive Nephrosclerosis	5D	no	Hypertension	7	HD	AV fistula
43	VK	259465	40	1	M	HD	hindu	urban	Diabetic Nephropathy	5D	YES LVEF 38%	Hypertension	13	HD	AV fistula
44	AK	405791	60	3	M	HD	hindu	urban	Diabetic Nephropathy	5D	no	Hypertension	9	HD	AV fistula
45	PK	138774	57	3	M	HD	hindu	urban	CIN CKD	5D	YES LVEF 40%	no	7	HD	AV fistula
46	PS	250820	57	3	M	HD	sikh	rural	Hypertensive Nephrosclerosis	5D	no	Hypertension	9	HD	AV fistula
47	BK	236049	51	2	F	IPD	sikh	rural	Hypertensive Nephrosclerosis	5	no	Hypertension	0	NAD	NAD
48	KK	139650	57	3	F	HD	hindu	urban	CIN CKD	5D	no	no	9	HD	AV fistula
49	NK	211071	64	4	M	HD	hindu	urban	Diabetic Nephropathy	5D	no	Hypertension	7	HD	AV fistula
50	DR	391339	60	3	F	HD	hindu	urban	Hypertensive Nephrosclerosis	5D	no	Hypertension	9	HD	AV fistula
51	MD	122053	48	2	M	OPD	hindu	urban	Diabetic Nephropathy	5	YES LVEF 38%	no	0	NAD	NAD
52	RK	444596	42	2	M	OPD	hindu	urban	Diabetic Nephropathy	5	no	Hypertension	0	NAD	NAD
53	BS	134197	69	4	M	OPD	sikh	rural	Hypertensive Nephrosclerosis	5	no	Hypertension	0	NAD	NAD
54	SR	215023	60	3	F	OPD	sikh	urban	Diabetic Nephropathy	5	no	no	0	NAD	NAD
55	RS	297928	70	4	F	OPD	hindu	urban	Hypertensive Nephrosclerosis	5	no	Hypertension	0	NAD	NAD
56	JS	268834	30	1	M	OPD	hindu	rural	Hypertensive Nephrosclerosis	4	no	Hypertension	0	NAD	NAD

S.NO.	Name	MRD	frequency per week	Aleondronate given by oral route	compliance to alondronate	erythropoietin therapy	weight in Kg	Height in cm	SBP	DBP	pallor	Skin manifestation	Hemoglobin baseline g/dl	Hemoglobin at 3 month	Hemoglobin at 6 months	Hemoglobin at 12 months	TLC baseline per ul	TLC at 3 months	TLC at 6 months	TLC at 12 months
1	DS	39091	2	yes	NAD	yes	59	166	130	80	yes	no	8.9	9.2	9.1	9	9.3	10.3	11.2	9.9
2	RS	95232	1	yes	good	yes	69	168	140	80	yes	no	9.9	9.8	9.9	9.7	10.3	11.3	11.7	7.9
3	NS	275234	1	No	NAD	yes	57.4	165	130	80	yes	no	8.9	9.2	9.1	10.1	8.3	10.5	11.2	9.9
4	SA	81489	2	No	NAD	yes	61	167	132	80	yes	no	10.3	9.4	9	9.8	6.3	10.4	7.3	10.6
5	NS	358756	0	yes	good	No	71	168	124	80	yes	no	11.1	11.1	11.5	10.9	7.4	10.6	6.3	10.2
6	HS	362450	2	yes	good	yes	104	176	138	80	yes	no	8.9	9.2	9.3	9.9	8.3	10.2	7.4	10.3
7	NJ	146147	3	yes	good	yes	96	171	130	90	yes	no	8.7	9.2	9.1	9.8	8.1	10.3	8.3	10.2
8	HS	84886	3	No	NAD	yes	76	169	130	80	yes	no	8.8	9.6	9.5	10.2	9.3	10.2	8.1	10.4
9	JS	372848	2	No	NAD	yes	61	168	134	86	yes	no	9.4	9.2	9.6	10	5.4	10.4	9.3	10
10	VA	192368	3	yes	good	yes	50.5	158	130	78	yes	no	10.4	9.7	9.3	9.8	8.2	10	5.4	10.4
11	HS	189874	2	No	NAD	yes	63	168	120	90	yes	no	8.9	9.2	9.1	9.7	7.3	10.4	8.2	8.3
12	RV	241271	2	No	NAD	yes	48	154	130	80	yes	no	9.2	9.3	9.4	9.8	6.6	8.3	7.3	8.1
13	JG	184776	2	No	NAD	yes	93	167	132	84	yes	no	9.1	9.2	9.5	9.6	7.7	8.1	6.6	9.3
14	RM	197400	2	yes	good	yes	64	170	120	70	yes	no	11.2	9.4	9.8	10	7.6	9.3	7.7	5.4
15	SK	115952	2	yes	good	yes	65	168	110	78	yes	no	10.2	9.2	9.7	9.8	7.2	5.4	7.6	9.9
16	SS	140578	2	No	NAD	yes	49	163	132	82	yes	no	10	9.8	9.1	9.6	7.3	8.2	7.2	10.6
17	BK	201967	3	yes	good	yes	55	168	128	86	yes	no	9.7	9.7	9.6	9.7	10.3	7.3	11.2	10.2
18	NK	43405	2	No	NAD	yes	57	155	134	90	yes	no	9.9	9.2	9.7	9.9	9.7	6.6	11.2	10.3
19	GS	198374	2	No	NAD	yes	59	159	120	70	yes	no	9.8	9.2	9.8	10.1	9.3	7.7	11.2	10.2
20	SK	371465	2	yes	good	yes	58	167	154	86	yes	no	9.1	9.5	9.1	10.2	10.4	7.2	6.9	10.4
21	AK	132172	2	yes	good	yes	54	165	130	80	yes	no	8.9	9.2	9.3	9.9	8.1	6.6	9.3	10
22	IS	191015	2	yes	good	yes	56	164	120	80	yes	no	8.7	9.2	9.1	9.8	9.3	7.7	5.4	10.4
23	RS	451663	0	No	NAD	yes	67	158	130	80	yes	no	8.8	9.6	9.5	10.2	5.4	7.6	9.9	8.3
24	AS	96083	2	No	NAD	yes	81	169	132	80	yes	no	9.4	9.2	9.6	10	8.2	7.2	10.6	8.1
25	HK	208490	2	yes	good	yes	63	168	124	80	yes	no	10.4	9.7	9.3	9.8	7.3	11.2	10.2	9.3
26	RC	23008	2	No	NAD	yes	62	169	138	80	yes	no	8.9	9.2	9.1	9.7	10.4	11.2	10.3	5.4
27	RS	182281	2	No	NAD	yes	71	166	130	80	yes	no	9.1	9.2	9.5	9.6	10.6	6.3	10.2	7.2
28	JS	151689	0	yes	good	yes	77	167	132	80	yes	no	8.9	9.2	9.1	9.7	10.2	7.4	10.3	5.3
29	NS	462800	0	No	NAD	yes	64	170	124	80	yes	no	9.4	9.2	9.6	10	10.3	8.3	10.2	10.3
30	GS	78322	0	yes	good	yes	52	168	138	80	yes	no	10.4	9.7	9.3	9.8	10.2	8.1	10.4	9.7
31	SP	413783	2	yes	good	yes	61	167	150	80	yes	yes	8.9	9.2	9.1	9.7	10.4	9.3	10	9.3
32	PK	415656	2	yes	good	yes	64	168	128	86	yes	yes	9.2	9.6	10	10.2	10	5.4	10.4	10.4
33	BK	236044	0	No	NAD	yes	57	163	130	80	yes	no	9.3	9.4	9.8	10	7.3	10.6	7.6	5.4
34	TK	209973	0	yes	good	yes	64	165	120	80	yes	no	9.2	9.5	9.6	9.7	6.3	10.2	7.2	8.2
35	KD	402541	0	No	NAD	yes	65	167	130	80	yes	no	9.6	9.5	10.2	11	7.3	10.6	5.3	8.2
36	SD	188308	0	No	NAD	yes	59	168	132	80	yes	no	9.2	9.1	9.7	10.5	6.3	10.2	10.3	7.3
37	GK	284262	2	yes	good	yes	55	166	140	90	yes	no	9.3	9.4	9.8	10.5	7.4	10.3	9.7	6.6
38	SS	135439	2	No	NAD	yes	62	168	132	84	yes	no	9.7	9.6	9.7	10.6	8.2	8.3	5.4	7.6
39	GS	184285	2	yes	good	yes	77	170	132	82	yes	no	9.2	9.8	9.1	9.2	9.7	6.6	11.2	10.3
40	SA	457442	2	No	NAD	yes	73	171	128	86	yes	no	9.3	9.1	9.4	8.9	9.3	7.7	11.2	10.2
41	GS	330245	2	yes	good	yes	52	159	130	80	yes	no	9.2	8.9	9.5	9.2	10.4	7.2	6.9	10.4
42	CK	393125	2	No	NAD	yes	71	168	144	88	yes	no	9.6	9.7	9.6	10.7	9.3	7.7	5.4	10.4
43	VK	259465	2	yes	good	yes	77	166	120	90	yes	no	8.8	9.6	9.5	10.2	5.4	7.6	9.9	8.3
44	AK	405791	2	yes	good	yes	73	171	130	80	yes	no	9.4	9.2	9.6	10	8.2	7.2	10.6	8.1
45	PK	138774	2	No	NAD	yes	52	169	132	84	yes	no	10.4	9.7	9.3	9.8	7.3	11.2	10.2	9.3
46	PS	250820	2	yes	good	yes	61	168	150	90	yes	no	8.9	9.2	9.1	9.7	10	8.1	8.1	10.2
47	BK	236049	0	No	NAD	yes	64	169	120	70	yes	no	9.2	9.3	9.4	9.8	10.4	9.3	9.3	10.3
48	KK	139650	2	No	NAD	yes	63	168	110	78	yes	no	8.9	9.2	9.1	9.7	8.3	5.4	5.4	10.2
49	NK	211071	2	No	NAD	yes	59	166	132	82	yes	no	9.2	9.3	9.4	9.8	8.1	8.2	8.1	10.4
50	DR	391339	2	No	NAD	yes	57	167	128	86	yes	no	8.9	9.2	9.3	9.9	9.6	11.2	9.3	8.1
51	MD	122053	0	yes	good	yes	64	170	130	80	yes	no	8.7	9.2	9.1	9.8	6.6	11.2	5.4	9.3
52	RK	444596	0	yes	good	yes	65	168	120	90	yes	yes	8.8	9.6	9.5	10.2	7.7	11.2	8.1	5.4
53	BS	134197	0	yes	good	yes	59	167	130	80	yes	yes	9.4	9.2	9.6	10	7.2	6.9	9.3	8.2
54	SR	215023	0	No	NAD	yes	55	168	132	84	yes	yes	10.4	9.7	9.3	9.8	6.6	9.3	5.4	10.2
55	RS	297928	0	yes	good	yes	57	166	120	70	yes	yes	8.9	9.2	9.1	9.7	10.2	8.1	10.4	9.7
56	JS	268834	0	No	NAD	yes	59	159	110	78	yes	yes	9.4	9.2	9.6	10	10.4	9.3	10	9.3

S.NO.	Name	MRD	Platelets at baseline lakh	Platelets at 3 months	Platelets at 6 months	Platelets at 12 months	ESR at baseline mm/first hr	Urea at baseline mg/dl	Urea at 3 months	Urea at 6 months	Urea at 12 months	CREATININE baseline mg/dl	Creatinine at 3 months	creatinine at 6 months	creatinine at 12 months	sodium baseline meq/l	sodium at 3 months	sodium at 6 months	sodium at 12 months	potassium at baseline meq/l	potassium at 3 months
1	DS	39091	1.98	2.1	2.1	2.13	17	150	149	158	152	4.9	3.7	4.9	6.5	137	131	138	136	5.5	4.9
2	RS	95232	1.54	1.12	2	2.3	15	156	184	153	159	5.9	3.6	3.9	3.5	138	133	139	134	4.5	3.9
3	NS	275234	1.6	1.34	2.4	1.34	17	115	149	138	122	3.8	4.7	3.9	4.8	137	136	138	136	6.5	4.6
4	SA	81489	1.28	1.46	1.76	1.33	18	121	116	98	149	3.9	5.7	6.9	2.9	124	133	138	126	4.3	3.8
5	NS	358756	1.76	1.43	1.64	1.98	17	132	157	139	156	2.6	2.7	2.8	2.9	143	138	138	141	3.8	2.9
6	HS	362450	2.98	1.39	1.98	1.8	15	92	119	116	115	3.8	2.9	3.9	4.9	135	138	137	132	2.9	5.3
7	NJ	146147	1.98	1.63	1.12	1.9	21	98	132	157	121	4.8	3.7	5.9	5.2	130	137	124	147	5.3	4.4
8	HS	84886	1.12	1.24	1.34	2.13	17	139	135	119	132	2.9	4.9	3.8	4.2	141	124	143	133	4.4	3.3
9	JS	372848	1.34	1.34	1.46	1.34	23	116	145	132	98	3.7	5.2	3.9	3.6	132	143	135	132	3.3	3.7
10	VA	192368	1.46	2.1	1.56	1.46	17	157	142	135	98	4.9	4.2	2.9	3.8	147	133	130	142	3.7	4.7
11	HS	189874	1.43	1.46	1.54	1.43	30	119	128	145	139	5.2	5.2	3.8	4.2	133	135	141	136	4.7	3.6
12	RV	241271	1.39	1.43	1.12	1.39	27	132	134	142	116	4.2	4.2	4.8	5.1	132	139	132	133	3.6	4.9
13	JG	184776	1.63	1.39	1.34	1.63	17	135	129	158	157	3.6	3.6	2.9	6.2	142	133	147	138	5.2	4.2
14	RM	197400	1.24	1.63	1.46	1.24	29	145	149	116	119	3.8	3.8	4.9	6.9	129	138	133	138	6.1	5.7
15	SK	115952	1.34	1.24	1.43	1.34	17	142	124	157	132	4.2	4.2	3.9	4.9	119	137	136	137	6.3	5.2
16	SS	140578	1.33	1.34	1.39	2.13	18	128	142	119	135	5.1	5.1	5.9	5.5	127	124	133	124	6	3.2
17	BK	201967	1.98	2.1	1.63	1.34	20	134	119	132	145	6.2	6.2	3.8	4.8	152	143	138	143	5.4	3.8
18	NK	43405	1.8	1.46	1.24	1.46	19	139	139	135	142	6.9	4.7	3.9	3.9	129	135	138	133	3.3	3.2
19	GS	198374	1.9	1.43	1.34	1.43	18	128	156	145	128	4.9	6.7	4.9	4.6	139	130	137	136	3.6	5.3
20	SK	371465	2.1	1.39	1.36	1.39	21	119	116	115	134	4.2	3.9	3.8	5.2	124	143	133	133	3.7	5.4
21	AK	132172	1.46	1.63	1.46	1.63	17	132	157	121	139	5.1	5.9	4.8	4.2	143	135	132	132	4.1	4.2
22	IS	191015	1.43	1.24	1.43	1.71	15	135	119	132	128	2.9	3.9	4.9	3.6	133	130	142	142	5.3	4.8
23	RS	451663	1.39	1.34	1.5	1.58	21	157	139	142	119	3.7	3.8	3.8	3.8	135	141	136	129	4.4	3.2
24	AS	96083	1.63	1.5	1.9	1.43	17	119	116	128	132	4.9	3.8	4.2	4.2	139	132	133	119	3.3	5.3
25	HK	208490	1.24	1.34	2.13	1.39	17	132	157	134	135	5.2	3.9	3.6	5.1	133	147	138	127	3.7	5.4
26	RC	23008	1.34	1.46	1.34	1.63	15	135	119	129	145	4.2	2.9	3.8	6.2	138	133	138	152	4.7	4.2
27	RS	182281	1.46	1.54	1.43	1.34	17	142	135	124	128	4.2	4.8	5.1	6.7	139	132	124	133	4.9	6.2
28	JS	151689	1.43	1.12	1.39	1.33	23	128	145	142	134	2.6	2.9	2.9	3.9	133	147	143	138	4.6	5.7
29	NS	462800	1.49	1.34	1.63	1.98	17	134	142	119	139	3.9	4.9	4.9	5.9	138	133	135	138	3.8	5.4
30	GS	78322	1.63	1.46	1.56	1.8	30	129	134	139	128	5.2	3.9	3.6	6.9	137	136	130	137	2.9	3.2
31	SP	413783	1.44	1.53	1.84	1.9	27	116	115	134	119	4.2	2.9	3.8	4.9	124	133	141	124	5.3	5.8
32	PK	415656	1.43	1.12	1.39	2.1	17	157	121	139	132	5.2	3.8	4.2	4.2	143	138	132	143	4.4	3.2
33	BK	236044	1.24	1.43	1.34	1.46	17	157	121	139	128	2	2.9	2.9	3.1	147	138	127	135	4.4	3.3
34	TK	209973	1.34	1.39	2.13	2.4	29	119	132	128	119	3.7	3.9	4.3	4.3	133	138	152	130	3.3	3.7
35	KD	402541	2.1	1.63	1.34	1.54	17	139	142	119	132	5.1	5.1	5.2	5.2	136	137	129	141	3.7	4.7
36	SD	188308	1.46	1.24	1.46	1.12	20	116	128	132	135	2.2	2.3	2.2	2.2	132	124	133	132	4.7	3.6
37	GK	284262	1.43	1.34	1.43	1.34	23	157	134	135	157	4.8	5.1	6.7	6.2	147	143	138	147	3.6	3.3
38	SS	135439	1.46	1.34	1.63	1.49	17	134	142	115	116	3.8	4.2	4.2	2.9	143	143	138	132	5.4	4.4
39	GS	184285	1.12	1.39	1.33	1.43	21	124	157	98	139	2.9	6.2	3.9	2.9	143	147	138	127	4.3	3.3
40	SA	457442	1.34	1.63	1.98	1.39	17	142	119	98	116	4.9	6.9	5.9	3.9	135	133	138	152	6	3.7
41	GS	330245	1.46	1.44	1.54	1.63	23	119	132	139	157	3.9	3.6	6.9	5.9	130	136	137	129	5.4	4.4
42	CK	393125	1.52	1.39	2.1	1.39	30	156	145	157	132	3.8	4.2	4.2	5.1	132	135	132	144	3.6	3.7
43	VK	259465	1.34	1.63	1.5	1.86	22	116	115	119	135	4.8	5.1	5.1	6.2	132	124	133	122	5.4	4.7
44	AK	405791	1.46	1.24	1.34	1.93	21	157	121	132	128	4.8	5.1	6.7	6.9	147	143	138	119	4.2	3.2
45	PK	138774	1.43	1.34	1.46	1.59	19	119	132	135	134	2.9	6.2	3.9	3.6	137	129	141	149	5.8	5.8
46	PS	250820	1.63	1.46	1.42	1.34	18	139	142	145	129	4.9	6.9	5.9	3.8	133	135	138	137	3.2	4.3
47	BK	236049	1.24	1.46	1.24	1.46	16	116	128	142	116	3.9	3.6	3.9	3.9	136	130	137	124	5.3	6
48	KK	139650	1.34	1.43	1.34	1.43	18	157	134	128	157	2.9	3.8	4.9	4.9	133	141	124	143	5.4	5.4
49	NK	211071	1.33	1.39	2.1	1.39	20	119	129	139	119	3.8	4.2	4.2	4.2	138	132	143	135	4.2	3.3
50	DR	391339	1.98	1.64	1.57	1.78	14	132	149	156	139	4.8	5.1	5.1	4.7	138	147	133	132	2.2	3.6
51	MD	122053	1.8	1.5	1.56	1.43	17	135	124	116	116	4.9	6.2	6.3	6.4	133	119	143	147	6.2	3.7
52	RK	444596	1.9	1.34	1.34	1.39	15	145	142	157	157	4.9	5.9	6	6.2	138	127	135	133	4.6	5.7
53	BS	134197	2.1	1.46	1.24	1.34	21	145	125	119	157	4.8	4.9	4.9	5.9	138	152	130	136	3.8	5.4
54	SR	215023	2.13	1.43	1.34	1.46	17	115	119	139	119	4.8	4.2	5.1	6.9	137	129	141	143	2.9	3.2
55	RS	297928	1.34	1.33	1.33	1.63	23	121	132	116	132	5.1	5.1	6.2	6.9	124	133	132	135	5.3	5.8
56	JS	268834	1.46	1.24	1.46	1.24	17	116	132	119	135	4.4	4.4	4.4	4.5	143	138	147	124	4.4	3.2

S.NO.	Name	MRD	potassium at 6 months	potassium at 12 months	Calcium baseline mg/dl	calcium at 3 months	calcium at 6 months	calcium at 12 months	phosphorus mg/dl baseline	phosphorus at 3 months	phosphorus at 6 months	phosphorus at 12 months	alakaline phosphotase base line U/dl	alkaline phosphatase at 3 months	alkaline phosphatase at 6 months	alkaline phosphatase at 12 months	Uric acid baseline mg/dl	uric acid at 3 months	uric acid at 6 months	uric acid at 12 months	Total protein mg/dl baseline
1	DS	39091	5.2	5.1	8.9	8.1	8.3	7.9	6.6	6.1	6.2	6	184	205	189	183	6.3	5.9	5.7	5.4	7
2	RS	95232	5.1	5.2	8.6	8.3	8	7.8	6.4	6.6	7.2	6.8	145	150	158	146	5.3	5.6	5.5	5.2	7.1
3	NS	275234	5.7	5.1	8.9	8.1	8.3	7.9	8.6	6.2	6.2	6.6	165	144	147	146	4.6	6.8	7.6	6.8	6.9
4	SA	81489	5.4	5.3	7.9	9.1	8.6	8.3	5.6	5.9	6.8	6.5	139	137	157	139	4.8	6.6	6.8	6.6	6.8
5	NS	358756	3.2	4.1	9.9	8.6	9.3	8.5	7.6	6.8	6.6	5.6	146	130	165	144	6.8	6.5	6.7	6.9	6.7
6	HS	362450	5.8	5.6	8.7	8.3	7.8	8.4	6.2	6.2	6.5	7.6	139	154	139	137	6.2	6.2	6.6	6.6	6.6
7	NJ	146147	3.2	5.2	7.9	8.8	8.3	8.3	5.6	6.2	5.6	6.2	144	164	146	138	5.9	6.8	6.5	6.4	6.8
8	HS	84886	5.3	5.7	8.6	9.6	8.5	8.6	8.6	6.1	7.6	5.9	137	159	139	165	6.8	6.6	5.6	8.6	6.7
9	JS	372848	5.4	5.1	8.5	8.6	8.4	7.9	10.6	5.6	6.2	6.8	130	162	144	139	6.2	6.5	7.6	5.6	6.8
10	VA	192368	4.2	3.8	7.9	8.4	8.3	9.9	7.6	7.6	5.9	6.4	154	137	137	126	6.2	5.6	6.2	7.6	6.7
11	HS	189874	2.2	2.9	8.3	8.8	8.6	8.7	6.8	6.2	6.8	8.6	164	130	130	139	6.1	7.6	5.9	6.2	6.6
12	RV	241271	6.2	5.3	8.5	9.3	8.3	7.9	6.9	5.6	6.2	5.6	159	165	154	144	5.6	6.2	6.8	5.6	6.8
13	JG	184776	5.2	4.4	8.4	7.8	8.7	8.6	6.5	6.1	6.2	7.6	162	139	164	137	6.2	5.7	5.5	5.8	6.7
14	RM	197400	5.6	3.3	8.3	8.3	7.9	8.5	6.2	6.7	5.6	6.2	160	146	144	130	6.3	5.8	5.6	5.4	6.8
15	SK	115952	4.6	3.7	8.6	8.5	8.6	7.9	6.7	7.2	8.6	5.6	157	139	137	124	6.2	5.6	5.7	5.8	6.7
16	SS	140578	3.8	5.6	8.8	8.4	8.5	8.3	11.6	6.2	10.6	9.8	149	144	130	146	4.6	6.8	7.6	6.8	6.9
17	BK	201967	2.9	5.8	8.4	10.1	7.9	7.9	4.6	6.8	7.6	6.8	145	137	154	142	4.8	6.6	6.8	6.6	5.7
18	NK	43405	5.3	5.9	9.9	7.1	8.3	8.1	4.8	6.6	6.8	6.6	139	164	164	144	6.8	6.5	6.7	6.9	5.9
19	GS	198374	4.4	4.1	9.2	8.9	7.9	8.3	6.8	6.5	6.7	6.9	138	159	159	137	6.2	6.2	6.6	6.6	6.9
20	SK	371465	3.3	3.6	8.1	8.6	8.9	8.1	6.2	6.2	6.6	6.6	139	162	162	148	5.9	6.8	6.5	6.4	5.2
21	AK	132172	3.7	5.2	8.3	8.7	7.8	9.4	5.9	6.8	6.5	6.4	144	160	137	122	6.8	6.6	5.6	8.6	6.2
22	IS	191015	4.7	6.1	9.1	8.6	8.3	7.8	6.8	6.6	5.6	8.6	137	157	162	164	6.2	6.5	7.6	5.6	6.3
23	RS	451663	3.6	6.3	8.6	9.3	8.5	8.3	6.2	6.5	7.6	5.6	150	158	168	144	6.2	5.6	6.2	7.6	6.5
24	AS	96083	3.6	6	8.3	7.8	8.4	8.5	6.2	5.6	6.2	7.6	144	147	146	137	6.1	7.6	5.9	6.2	6.7
25	HK	208490	4.9	5.4	8.8	8.3	8.3	8.4	6.1	7.6	5.9	6.2	137	157	139	130	5.6	6.2	6.8	5.6	6.8
26	RC	23008	4.2	3.3	9.6	8.5	8.6	10.1	5.6	6.2	6.8	5.6	130	165	144	154	6.8	6.6	5.6	8.6	6.7
27	RS	182281	5.4	5.8	8.4	8.3	9.9	8.9	6.2	6.5	7.6	10.6	164	146	130	159	6.8	6.5	6.4	6.6	6.6
28	JS	151689	3.2	3.2	8.8	8.6	8.7	9.4	6.2	5.6	6.2	7.6	159	139	165	154	6.6	5.6	8.6	6.5	6.8
29	NS	462800	5.8	5.3	9.3	8.3	7.9	8.6	6.1	7.6	5.9	6	162	144	139	137	6.5	7.6	5.6	7.6	6.7
30	GS	78322	4.3	5.4	8.4	8.3	9.9	8.1	5.6	6.2	6.8	6.9	137	137	146	162	5.6	6.2	7.6	6.2	6.9
31	SP	413783	6	4.2	8.8	8.6	8.7	9.1	7.6	5.9	6.4	7.5	130	130	139	129	7.6	5.9	6.2	5.9	6.9
32	PK	415656	5.4	2.2	9.3	8.3	7.9	8.6	6.2	5.6	6.8	6.5	137	157	139	134	6.2	6.8	5.6	6.8	6.5
33	BK	236044	3.7	5.4	8.5	8.6	7.9	9.6	7.6	5.9	5.6	6.2	164	146	130	137	5.6	5.7	5.8	6.4	6.1
34	TK	209973	4.1	3.2	8.4	8.5	8.3	8.6	6.2	6.8	7.6	5.9	159	139	165	130	6.8	7.6	6.8	8.6	5.2
35	KD	402541	5.3	5.8	7.9	8.5	8.5	8.4	5.6	6.2	6.2	6.3	162	144	139	137	6.6	6.8	6.6	5.6	6.2
36	SD	188308	4.4	4.2	8.6	7.9	8.4	8.8	6.1	6.2	6.6	5.6	137	137	146	130	6.5	6.7	6.9	7.6	6.3
37	GK	284262	3.2	2.2	8.5	8.3	10.1	9.3	6.7	5.6	6.5	7.6	130	130	139	124	7.9	9.1	8.6	8.3	6.5
38	SS	135439	3.2	4.8	7.8	9.4	8.6	10.1	5.6	5.9	6.2	10.6	160	137	147	165	8.5	8.6	8.4	7.9	6.5
39	GS	184285	4.7	3.6	8.4	8.5	8.3	8.7	5.9	6.2	6.5	6.7	147	146	139	139	8.5	9.3	8.3	7.9	6.1
40	SA	457442	3.6	3.3	8.3	8.4	8.5	7.9	5.6	5.6	6.2	6.6	157	139	146	144	9.3	7.8	8.3	10.3	5.2
41	GS	330245	4.9	3.6	9.7	9.5	8.4	8.6	6.2	6.8	5.6	6.6	165	144	139	137	8.6	7.9	9.6	7.9	6.2
42	CK	393125	3.8	2.9	8.3	7.8	8.4	7.9	6.5	7.6	10.6	5.6	146	130	137	159	8.5	8.5	8.4	7.9	6.7
43	VK	259465	2.9	5.3	8.8	8.3	8.3	8.3	5.6	6.2	7.6	7.6	139	165	130	124	7.9	8.4	8.8	8.1	6.6
44	AK	405791	3.2	4.4	9.6	8.5	8.6	8.5	7.6	5.9	6.8	6.2	144	139	157	132	8.3	10.1	9.3	8.3	6.8
45	PK	138774	5.3	3.3	8.6	8.4	7.9	7.9	6.2	6.8	6.9	6.6	137	146	165	162	7.9	7.1	7.8	8.1	6.7
46	PS	250820	5.4	3.7	8.4	8.3	9.9	8.3	5.9	6.4	7.5	5.9	137	156	139	128	7.9	9.1	8.6	8.3	6.8
47	BK	236049	4.2	4.4	8.8	8.6	8.7	7.9	5.6	6.8	6.5	6.2	130	144	147	146	9.9	8.6	9.3	8.5	6.6
48	KK	139650	2.2	5.3	9.3	8.3	7.9	8.9	6.8	8.6	6.2	6.8	154	137	157	139	8.7	8.3	7.8	8.4	6.8
49	NK	211071	6.2	3.3	7.8	8.7	8.6	7.8	6.2	5.6	5.9	6.4	164	130	165	144	7.9	8.8	8.3	8.3	6.7
50	DR	391339	5.7	3.7	9.3	7.8	8.3	10.3	6.2	7.6	5.6	6.8	144	154	139	137	8.6	9.6	8.5	8.6	6.7
51	MD	122053	5.4	4.4	8.6	7.9	9.6	7.9	5.6	6.2	7.6	6.6	162	164	146	130	8.5	8.6	8.4	7.9	6.9
52	RK	444596	5.8	3.3	8.5	8.3	8.6	8.3	8.6	5.6	6.2	6.5	137	159	139	165	7.9	8.4	8.3	9.9	6.9
53	BS	134197	4.3	3.7	8.5	8.5	8.4	7.9	10.6	9.8	5.9	5.6	162	162	144	139	8.3	8.8	8.6	8.7	6.5
54	SR	215023	6	4.7	7.9	8.4	8.8	8.1	7.6	6.8	6.8	5.8	168	137	137	146	8.5	9.3	8.3	7.9	5.2
55	RS	297928	5.4	3.6	8.3	10.1	9.3	8.3	6.8	6.6	6.2	6.2	146	130	130	139	8.4	7.8	8.7	8.6	6.2
56	JS	268834	3.3	3.6	7.9	7.1	7.8	8.1	6.7	6.9	6.2	6.6	164	137	157	139	5.7	5.8	6.4	7.1	6.3

S.NO.	Name	MRD	Total protein at 3 months	Total protein at 6 months	Total protein at 12 months	Albumin mg/dl baseline	Albumin at 3 months	Albumin at 6 months	Albumin at 12 months	SGOT U/L baseline	SGOT at 3 months	SGOT at 6 months	SGOT at 12 months	SGPT U/L baseline	SGPT at 3 months	SGPT at 6 months	SGPT at 12 months	Total bilirubin mg/dl baseline	Total bilirubin at 3 months	Total bilirubin at 6 months	Total bilirubin at 12 months	IPTH pg/ml baseline	iPTH at 3 months	iPTH at 6 months
1	DS	39091	6.9	6.8	7.2	3.6	3.2	3.8	3.6	21	23	24	21	25	26	23	25	0.9	0.8	0.5	0.5	210	206	213
2	RS	95232	6.6	6.7	6.6	3.7	3.1	3.7	3.2	20	22	22	24	21	24	22	23	0.7	0.5	0.6	0.4	187	198	169
3	NS	275234	6.8	6.6	6.8	3.8	3.5	3.7	3.9	21	19	21	21	25	26	23	25	0.6	0.4	0.5	0.7	216	165	178
4	SA	81489	6.9	6.8	6.9	3.7	3.9	3.8	3.9	18	16	28	21	21	21	21	21	0.8	0.7	0.4	0.6	190	206	213
5	NS	358756	6.6	6.7	6.6	3.4	3.7	3.7	3.9	19	21	21	21	20	20	20	20	0.5	0.6	0.5	0.9	180	178	182
6	HS	362450	6.8	6.8	6.8	3.5	3.8	3.4	3.9	16	22	23	20	21	21	21	21	0.4	0.9	0.5	0.7	206	213	211
7	NJ	146147	6.9	6.7	6.9	3.9	3.7	3.5	3.9	21	21	19	21	18	18	18	18	0.7	0.5	0.4	0.6	198	169	176
8	HS	84886	6.8	6.9	6.8	3.7	3.4	3.8	3.9	22	28	24	18	19	19	19	19	0.6	0.3	0.7	0.8	165	178	189
9	JS	372848	6.7	6.6	6.9	3.8	3.5	3.7	3.9	21	21	21	19	16	16	16	16	0.9	0.8	0.6	0.5	206	213	205
10	VA	192368	6.9	6.8	6.6	3.7	3.2	3.4	3.9	28	20	22	16	21	21	21	21	0.7	0.9	0.9	0.4	178	182	192
11	HS	189874	6.9	6.7	6.8	3.4	3.8	3.5	3.9	21	21	21	21	22	22	22	22	0.6	0.7	0.7	0.7	206	213	205
12	RV	241271	6.5	6.8	6.9	3.5	3.7	3.9	3.9	23	18	28	22	21	21	21	19	0.8	0.6	0.6	0.6	178	182	192
13	JG	184776	6.9	6.7	6.8	3.9	3.4	3.7	3.9	19	19	24	21	28	28	28	16	0.5	0.8	0.8	0.8	213	211	212
14	RM	197400	5.9	6.8	6.7	3.7	3.5	3.8	3.9	16	16	21	28	21	21	21	21	0.4	0.5	0.5	0.8	169	176	178
15	SK	115952	6.1	6.6	6.7	3.7	3.9	3.7	3.9	21	21	20	21	23	23	23	16	0.7	0.4	0.4	0.8	178	189	192
16	SS	140578	5.2	6.8	6.6	3.8	3.7	3.1	3.9	22	22	21	23	19	19	19	21	0.6	0.7	0.7	0.9	206	213	211
17	BK	201967	6.2	6.9	6.8	3.7	3.8	3.9	3.9	21	19	18	19	16	16	16	22	0.9	0.6	0.6	0.7	198	169	176
18	NK	43405	6.3	6.8	6.7	3.4	3.7	3.9	3.9	28	16	19	16	21	21	21	21	0.5	0.9	0.5	0.6	165	178	189
19	GS	198374	6.5	6.7	6.8	3.5	3.1	3.7	3.9	21	21	16	21	22	22	22	28	0.3	0.8	0.5	0.7	206	213	205
20	SK	371465	6.7	6.1	6.6	3.5	3.5	3.8	3.7	19	16	20	22	21	21	21	21	0.4	0.8	0.6	0.8	206	213	205
21	AK	132172	6.9	5.2	6.8	3.7	3.2	3.7	3.8	16	21	21	21	28	28	28	25	0.7	0.5	0.9	0.7	178	182	192
22	IS	191015	5.7	6.2	6.9	3.4	3.8	3.4	3.7	21	22	22	28	21	21	21	23	0.6	0.4	0.7	0.6	213	211	212
23	RS	451663	6.7	6.8	6.9	3.5	3.7	3.1	3.4	22	21	21	21	16	21	21	21	0.9	0.7	0.6	0.8	169	176	178
24	AS	96083	6.8	6.7	6.6	3.9	3.4	3.5	3.5	21	28	28	21	21	21	23	20	0.7	0.6	0.8	0.5	178	189	192
25	HK	208490	6.7	6.9	6.8	3.7	3.5	3.5	3.9	28	21	21	22	23	22	23	22	0.6	0.9	0.4	0.4	213	205	204
26	RC	23008	6.6	6.9	6.7	3.4	3.8	3.7	3.7	22	23	21	21	19	21	19	21	0.8	0.7	0.7	0.7	182	192	207
27	RS	182281	6.7	6.9	6.7	3.2	3.4	3.7	3.7	28	24	21	21	21	21	21	23	0.4	0.8	0.9	0.5	182	192	198
28	JS	151689	6.8	5.9	6.8	3.8	3.5	3.4	3.4	21	21	21	20	22	20	22	19	0.8	0.5	0.7	0.4	169	176	178
29	NS	462800	6.6	6.9	5.2	3.7	3.6	3.1	3.5	20	22	19	21	21	21	21	24	0.5	0.4	0.6	0.7	178	189	192
30	GS	78322	6.8	6.6	6.2	3.4	3.7	3.6	3.5	21	21	20	18	28	18	28	21	0.4	0.7	0.8	0.6	213	205	204
31	SP	413783	6.7	6.8	6.3	3.5	3.8	3.6	3.5	18	28	21	19	24	19	24	22	0.7	0.6	0.5	0.9	182	192	207
32	PK	415656	6.8	6.9	6.5	3.9	3.7	3.8	3.7	19	24	22	16	21	16	21	21	0.6	0.9	0.4	0.7	213	205	210
33	BK	236044	6.6	6.7	5.7	3.2	3.7	3.8	3.9	22	21	21	19	18	19	18	21	0.6	0.8	0.5	0.5	176	178	187
34	TK	209973	6.8	6.6	6.7	3.8	3.4	3.7	3.9	19	18	23	16	19	16	19	20	0.8	0.7	0.4	0.4	189	192	198
35	KD	402541	6.9	6.8	6.8	3.7	3.1	3.4	3.7	16	19	19	21	16	21	16	24	0.5	0.6	0.6	0.6	182	192	207
36	SD	188308	6.8	6.7	6.7	3.2	3.4	3.7	3.8	21	16	16	19	21	21	21	21	0.4	0.5	0.5	0.7	213	205	210
37	GK	284262	6.7	6.8	5.9	3.8	3.5	3.4	3.7	21	21	21	16	22	23	22	22	0.7	0.7	0.4	0.6	182	192	198
38	SS	135439	6.8	6.9	6.9	3.4	3.5	3.5	3.2	21	21	21	21	21	21	16	21	0.6	0.5	0.6	0.6	192	182	192
39	GS	184285	6.6	6.7	6.7	3.7	3.5	3.8	3.2	21	19	21	21	21	21	18	19	0.6	0.6	0.4	0.6	197	213	205
40	SA	457442	6.8	6.6	6.9	3.4	3.4	3.7	3.8	28	24	21	18	20	22	19	16	0.8	0.9	0.4	0.8	193	182	192
41	GS	330245	6.9	6.8	6.9	3.5	3.6	3.4	3.7	21	21	22	19	21	21	16	23	0.5	0.7	0.7	0.5	230	213	205
42	CK	393125	6.9	6.8	6.3	3.9	3.4	3.5	3.5	21	21	28	21	19	24	22	24	0.6	0.7	0.4	0.9	245	211	212
43	VK	259465	6.9	6.7	6.5	3.7	3.3	3.5	3.1	18	28	21	22	16	21	21	21	0.9	0.6	0.7	0.7	194	176	178
44	AK	405791	6.5	6.8	6.8	3.8	3.5	3.5	3.4	19	24	21	21	21	20	28	22	0.5	0.9	0.6	0.6	189	192	175
45	PK	138774	6.9	6.7	6.7	3.7	3.9	3.7	3.5	16	21	20	28	22	21	21	21	0.7	0.4	0.4	0.8	205	204	198
46	PS	250820	5.9	6.8	6.9	3.7	3.6	3.8	3.9	21	20	21	21	19	18	23	28	0.6	0.7	0.7	0.9	192	207	213
47	BK	236049	6.9	5.2	6.9	3.8	3.7	3.5	3.7	22	21	18	23	16	19	19	24	0.6	0.7	0.7	0.7	205	210	169
48	KK	139650	6.6	6.2	6.5	3.7	3.8	3.9	3.8	19	18	19	19	21	16	16	21	0.8	0.6	0.6	0.6	192	198	178
49	NK	211071	6.8	6.3	6.9	3.4	3.7	3.9	3.1	16	19	16	16	20	22	19	20	0.5	0.8	0.8	0.8	212	202	205
50	DR	391339	6.6	6.2	5.9	3.1	3.4	3.7	3.5	21	16	21	21	21	21	16	21	0.4	0.5	0.5	0.8	178	187	192
51	MD	122053	6.8	6.3	6.7	3.4	3.9	3.8	3.4	20	22	19	22	18	28	21	22	0.7	0.4	0.4	0.8	192	198	205
52	RK	444596	6.7	6.5	6.8	3.5	3.9	3.7	3.6	21	21	21	21	19	24	22	21	0.6	0.7	0.7	0.9	192	207	190
53	BS	134197	6.8	6.8	5.2	3.5	3.7	3.9	3.7	18	28	21	28	16	21	21	28	0.9	0.6	0.6	0.7	205	210	194
54	SR	215023	6.7	6.6	6.7	3.9	3.8	3.7	3.1	19	24	22	21	23	21	19	21	0.5	0.9	0.5	0.6	192	198	178
55	RS	297928	6.6	6.8	6.8	3.7	3.7	3.8	3.5	16	21	21	23	19	23	16	24	0.3	0.8	0.5	0.7	212	202	189
56	JS	268834	6.8	6.9	6.7	3.8	3.4	3.7	3.9	19	21	21	19	24	19	21	21	0.6	0.3	0.7	0.8	178	187	168

S.NO.	Name	MRD	iPTH at 12 months	vitamin D3 ng/ml baseline	vitamin D3 at 3 months	vitamin D3 at 6 months	vitamin D3 at 12 months	Fracture at Xray DL spine at baseline	Fracture at Xray DL spine at 12 months	Fracture at Xray DL spine at 12 months	fracture in chest X ray at baseline	fracture in chest X ray at 6 months	fracture in chest X ray at 12 months	fracture in X ray hand at baseline	fracture in X ray hand at 6 months	fracture in X ray hand at 12 months	subperiosteal resorbtion of phalanges on x ray hand	calcification of abdominal aorta on x ray of lumbar spine	lumbar spine T score baseline	lumbar spine T score 6 months	lumbar spine T score 12 months
1	DS	39091	211	26	22	20	23	no	no	no	no	no	no	no	no	no	NO	NO	-1.4	-1.5	-1.2
2	RS	95232	170	22	26	31	30	no	no	no	no	no	no	no	no	no	yes	yes	-1.6	-1.4	-1.2
3	NS	275234	189	23	30	30	26	yes	yes	yes	no	no	no	no	no	no	yes	yes	-4	-4.1	-4.3
4	SA	81489	205	14	30	31	26	no	no	no	no	no	no	no	no	no	NO	NO	-1.42	-1.49	-1.79
5	NS	358756	176	24	24	28	24	no	no	no	no	no	no	no	no	no	NO	NO	-2.1	-2	-1.79
6	HS	362450	212	28	28	26	25	no	no	no	no	no	no	no	no	no	NO	NO	-0.5	-0.4	-0.2
7	NJ	146147	178	30	30	26	27	no	no	no	no	no	no	no	no	no	NO	NO	-0.5	-0.4	-0.2
8	HS	84886	192	31	31	24	30	no	no	no	no	no	no	no	no	no	NO	NO	-1.34	-1.52	-1.61
9	JS	372848	204	28	28	25	23	no	no	no	no	no	no	no	no	no	NO	NO	-1.7	-1.8	-1.9
10	VA	192368	190	26	26	27	22	yes	yes	yes	no	no	no	no	no	no	yes	yes	-3	-2.9	-2.5
11	HS	189874	210	26	26	30	28	no	no	no	no	no	no	no	no	no	NO	NO	-1.6	-1.7	-1.8
12	RV	241271	198	24	24	23	22	no	no	no	no	no	no	no	no	no	NO	yes	-1.3	-1.5	-1.7
13	JG	184776	202	25	25	22	27	no	no	no	no	no	no	no	no	no	yes	yes	-1.5	-1.6	-1.6
14	RM	197400	170	27	27	28	26	no	no	no	no	no	no	no	no	no	NO	NO	-2	-1.9	-1.9
15	SK	115952	188	30	30	26	22	no	no	no	no	no	no	no	no	no	NO	NO	-4.1	-3.9	-3.1
16	SS	140578	203	23	23	24	23	no	no	no	no	no	no	no	no	no	NO	NO	0.3	0.2	0.2
17	BK	201967	168	22	22	25	14	no	no	no	no	no	no	no	no	no	NO	NO	-2.4	-2.1	-2
18	NK	43405	175	28	26	27	30	no	no	no	no	no	no	no	no	no	NO	NO	-1.5	-1.6	-1.7
19	GS	198374	198	22	24	26	26	no	no	no	no	no	no	no	no	no	yes	yes	-3.2	-3.3	-3.4
20	SK	371465	198	27	24	28	26	no	no	no	no	no	no	no	no	no	NO	NO	0.25	0.29	0.3
21	AK	132172	169	26	28	30	24	no	no	no	no	no	no	no	no	no	NO	NO	-1	-0.99	-0.9
22	IS	191015	178	22	30	31	25	no	no	no	no	no	no	no	no	no	NO	NO	0.2	0.4	0.45
23	RS	451663	213	23	31	28	27	no	no	no	no	no	no	no	no	no	NO	NO	-1.6	-1.7	-1.9
24	AS	96083	182	14	28	26	30	no	no	no	no	no	no	no	no	no	NO	NO	-1.5	-1.6	-1.6
25	HK	208490	197	24	26	26	23	no	no	no	no	no	no	no	no	no	NO	NO	-2.2	-2	-2
26	RC	23008	182	28	26	24	22	no	no	no	no	no	no	no	no	no	NO	NO	-2.7	-2.8	-2.9
27	RS	182281	179	31	25	27	22	no	no	no	no	no	no	no	no	no	NO	NO	-0.6	-0.6	-0.7
28	JS	151689	158	28	27	30	27	no	no	no	no	no	no	no	no	no	NO	NO	-0.5	-0.4	-0.3
29	NS	462800	175	26	30	23	26	no	no	no	no	no	no	no	no	no	yes	yes	-1.6	-1.6	-1.7
30	GS	78322	188	26	23	22	22	no	no	no	no	no	no	no	no	no	NO	NO	-1.5	-1.3	-1.2
31	SP	413783	206	24	28	28	23	no	no	no	no	no	no	no	no	no	NO	NO	-1.7	-1.6	-1.5
32	PK	415656	169	25	26	22	14	no	no	no	no	no	no	no	no	no	NO	NO	-4	-3.8	-3.6
33	BK	236044	192	23	30	31	30	no	no	no	no	no	no	no	no	no	NO	NO	0.6	0.5	0.3
34	TK	209973	184	22	23	28	23	no	no	no	no	no	no	no	no	no	NO	NO	-2.2	-2.1	-2
35	KD	402541	190	28	22	26	22	no	no	no	no	no	no	no	no	no	NO	NO	-0.7	-0.8	-0.81
36	SD	188308	194	27	28	26	28	no	no	no	no	no	no	no	no	no	NO	NO	0.4	0.3	0.2
37	GK	284262	178	26	22	24	22	no	no	no	no	no	no	no	no	no	NO	NO	-1.1	-0.9	-0.7
38	SS	135439	198	30	26	26	26	no	no	no	no	no	no	no	no	no	NO	NO	-2.9	-3	-3.1
39	GS	184285	204	28	27	27	27	no	no	no	no	no	no	no	no	no	NO	NO	1	1.3	1.39
40	SA	457442	207	22	30	30	30	no	no	no	no	no	no	no	no	no	NO	NO	-1.4	-1.4	-1.5
41	GS	330245	196	27	23	23	22	no	no	no	no	no	no	no	no	no	NO	NO	-2.1	-2	-1.8
42	CK	393125	202	22	26	28	26	yes	yes	yes	no	no	no	no	no	no	NO	NO	-4.6	-4.8	-5
43	VK	259465	176	23	25	22	24	no	no	no	no	no	no	no	no	no	NO	NO	-1.7	-1.6	-1.5
44	AK	405791	176	14	27	27	25	no	no	no	no	no	no	no	no	no	NO	NO	0.5	0.6	0.7
45	PK	138774	189	24	30	26	27	no	no	no	no	no	no	no	no	no	NO	NO	-0.9	-1	-1
46	PS	250820	213	22	21	22	30	no	no	no	no	no	no	no	no	no	NO	NO	-0.2	-0.1	-0.009
47	BK	236049	192	27	23	23	23	no	no	no	no	no	no	no	no	no	NO	NO	-2	-2.2	-2.4
48	KK	139650	172	26	24	14	22	no	no	no	no	no	no	no	no	no	NO	NO	-2.5	-2.6	-2.7
49	NK	211071	187	22	18	24	28	no	no	no	no	no	no	no	no	no	NO	NO	-0.4	-0.5	-0.7
50	DR	391339	197	22	30	30	30	no	no	no	no	no	no	no	no	no	NO	NO	-2.5	-3.6	-4
51	MD	122053	190	27	23	23	22	no	no	no	no	no	no	no	no	no	NO	NO	-1.8	-1.5	-1.3
52	RK	444596	178	26	28	22	26	no	no	no	no	no	no	no	no	no	NO	NO	-3.4	-3.3	-3.1
53	BS	134197	184	28	26	24	22	no	no	no	no	no	no	no	no	no	NO	NO	-3.5	-3.2	-3
54	SR	215023	172	30	24	25	22	no	no	no	no	no	no	no	no	no	NO	NO	-2.6	-2.7	-2.8
55	RS	297928	178	31	25	27	27	no	no	no	no	no	no	no	no	no	NO	NO	-0.8	-0.7	-0.5
56	JS	268834	167	28	27	30	26	no	no	no	no	no	no	no	no	no	NO	NO	-2.3	-2.4	-2.6

S.NO.	Name	MRD	lumbar spine Z score baseline	lumbar spine Z score at 6 months	lumbar spine Z score at 12 months	Lumbar spine Bone mineral density baseline g/m2	Lumbar spine Bone mineral density at 6 months	Lumbar spine Bone mineral density at 12months	femur neck T score baseline	femur neck T score at 6 months	femur neck T score at 12 months	femur neck Z score baseline	femur neck Z score at 6 months	femur neck Z score at 12 months	bone mineral density g/m2 baseline at femur neck	bone mineral density at 6 months at femur neck	bone mineral density 12 months at femur neck	Total hip T score at baseline	Total hip T score at 6 months	Total hip T score at 12 months	Total hip Z score at baseline	Total hip Z score at 6 months
1	DS	39091	0.5	0.49	0.4	1.12	1.1	1.046	-1.5	-1.5	-1.4	0.5	0.4	0.3	1.046	1.018	1.006	-2.4	-2.3	-2.2	1.5	1.34
2	RS	95232	0.1	0.09	0.09	1.51	1.56	1.64	-1.2	-1.1	-0.9	0.1	0.09	0.07	0.804	0.99	0.99	-0.7	-0.4	-0.29	-0.1	-0.099
3	NS	275234	-2.8	-2.8	-2.8	0.741	0.738	0.732	-2.6	-2.7	-2.9	-2.5	-2.5	-2.6	0.745	0.74	0.726	-2	-2.4	-2.59	-0.9	-0.9
4	SA	81489	-0.5	-0.6	-0.69	1.047	1.023	1.007	-2.3	-2.5	-2.6	-0.4	-0.6	-0.6	0.77	0.677	0.567	-1.6	-1.7	-1.87	-0.7	-0.78
5	NS	358756	-2.2	-2.1	-2.09	0.974	1.2	1.25	-2.1	-1.8	-1.6	-2	-2	-1.8	0.797	0.799	1.897	-1.2	-1.19	-1.009	-1	-0.9
6	HS	362450	-1	-0.9	0.8	1.15	1.21	1.31	0.6	0.5	0.6	-1	-0.9	-0.7	1.232	1.31	1.329	-2.5	-2.1	-2	-2.6	-2.3
7	NJ	146147	-0.3	-0.2	-0.1	1.18	1.21	1.33	-2.1	-2	-1.8	-0.4	-0.2	-0.1	0.91	0.99	1.1	-1.4	-1.3	-1.2	-1.5	-1.1
8	HS	84886	0.52	0.49	0.43	1.128	1.102	1.046	-1.53	-1.55	-1.64	0.5	0.4	0.3	1.056	1.015	1.008	-2.3	-2.4	-2.6	1.52	1.34
9	JS	372848	0.56	0.44	0.42	1.42	1.28	1.036	-1.2	-1.28	-1.4	0.6	0.4	0.3	1.228	1.22	1.11	-2.4	-2.4	-2.5	2.8	2.7
10	VA	192368	-1.6	-1.41	-1.39	0.825	0.88	1.1	-3.6	-3.4	-3.2	-1.6	-1.5	-1.3	0.51	0.59	0.61	-3.4	-3.1	-2.8	-2.3	-2.2
11	HS	189874	0.57	0.46	0.41	1.324	1.3	1.086	-1.6	-1.5	-1.7	0.5	0.46	0.41	1.159	1.15	1.008	-1.8	-2	-2.1	-0.2	-0.26
12	RV	241271	-0.5	-0.49	-0.5	1.023	1.013	1.002	-2	-2.2	-2.4	-0.5	-0.5	-0.6	0.788	0.72	0.702	-1.4	-1.5	-1.8	-0.6	-0.7
13	JG	184776	-0.9	-0.98	-0.99	1.36	1.33	1.31	-2	-2.23	-2.4	-0.9	-0.9	-1	1.11	1.118	1.107	-2	-2.02	-2.2	-2	-2.2
14	RM	197400	-0.8	-0.7	-0.5	1.12	1.245	1.328	-1.7	-1.5	-1.1	-0.8	-0.7	-0.6	1.64	1.728	1.908	-2.4	-2.3	-2.2	-0.8	-0.6
15	SK	115952	-3.5	-3.4	-3	0.725	0.81	0.88	-2.9	-2.49	-2.32	-3	-3.2	-3	0.629	0.71	0.8	-2.1	-2	-2	-1.9	-1.7
16	SS	140578	-0.1	-0.1	-0.1	1.25	1.21	1.19	-2.9	-2.5	-2.5	-0.2	-0.1	-0.1	0.72	0.71	0.714	-1.7	-1.8	-1.8	-1.8	-1.6
17	BK	201967	-1.4	-1.3	-1.3	0.89	0.91	0.93	-2	-1.9	-1.7	-1.4	-1.3	-1.2	0.756	0.81	0.989	-2	-1.9	-1.6	-1.1	-0.9
18	NK	43405	0.5	0.49	0.4	1.318	1.3	1.146	-1.5	-1.6	-1.7	0.5	0.4	0.4	0.812	0.8	0.768	-0.8	-0.9	-2	-0.2	-0.3
19	GS	198374	-2.5	-2.6	-2.7	0.835	0.828	0.79	-2.9	-2.9	-2.9	-2.5	-2.5	-2.7	0.81	0.76	0.74	-2.6	-2.7	-2.2	-2.3	-2.3
20	SK	371465	1.9	2	2.1	1.22	1.3	1.35	0.1	0.2	0.5	1.8	2	2.1	1.154	1.21	1.31	-2.2	-2.1	-1.9	-0.9	-0.8
21	AK	132172	0.1	0.2	0.2	1.099	1.12	1.299	-3.9	-3.2	-3.1	0.1	0.1	0.2	0.569	0.698	0.789	-3.1	-3	-2.9	-2.1	-1.99
22	IS	191015	1.1	1.29	1.3	1.241	1.33	1.39	-2.5	-2.49	-2.2	1.1	1.2	1.3	0.748	0.79	0.891	-2.3	-2.2	-2.1	-1.3	-1.1
23	RS	451663	0.7	0.5	0.5	1.552	1.5	1.43	-1.4	-1.5	-1.5	0.7	0.6	0.5	0.91	0.899	0.825	-1	-0.9	-0.9	-0.3	-0.3
24	AS	96083	0.9	0.8	0.7	1.383	1.3	1.21	-0.1	-0.6	-0.6	1	0.8	0.7	1.1	1.09	1.064	-0.3	-0.3	-0.5	0.5	0.4
25	HK	208490	-2	-1.9	-1.8	0.906	0.989	0.99	-3.2	-3.1	-2.7	-2	-1.9	-1.7	0.6	0.678	0.789	-2.7	-2.6	-2.5	-2.3	-2.2
26	RC	23008	-1.6	-1.7	-1.7	0.9	0.87	0.789	-2.9	-2.9	-3	-1.6	-1.7	-1.8	0.69	0.598	0.558	-1.8	-1.9	-1.9	-1	-1.1
27	RS	182281	0.7	0.6	0.5	1.19	1.045	1.038	-3.3	-3.4	-3.7	0.7	0.6	0.4	0.69	0.63	0.629	-2.2	-2.3	-2.4	-1.2	-1.3
28	JS	151689	-0.2	-0.1	-0.099	1.22	1.3	1.38	-0.2	-0.1	-0.1	-0.2	-0.1	-0.09	1.06	1.08	1.18	-1.3	-1	-0.5	0.4	0.5
29	NS	462800	1.4	1.4	1.3	1.417	1.39	1.29	-0.5	-0.6	-0.6	1.5	1.4	1.3	1.109	1.009	1.003	0.3	0.2	0.1	0.4	0.3
30	GS	78322	-1.2	-1.1	-1.1	1.15	1.23	1.328	-0.3	-0.2	-0.1	-1.2	-1.1	-1	1.058	1.58	1.6	-0.8	-0.7	-0.6	-0.2	-0.2
31	SP	413783	-0.4	-0.3	-0.2	1.04	1.1	1.29	-3	-2.9	-2.8	-0.4	-0.3	-0.1	0.674	0.689	0.78	-2.4	-2.3	-2.1	-1.7	-1.1
32	PK	415656	-2.6	-2.4	-2.2	0.704	0.778	0.878	-2.8	-2.6	-2.4	-2.5	-2.4	-2.2	0.685	0.698	0.738	-2.2	-2	-1.9	-1.1	-1
33	BK	236044	1.2	1.1	1.1	1.253	1.2	1.18	-1.5	-1.6	-1.7	1.2	1.1	1	1.2	0.99	0.968	-0.3	-0.4	-0.5	0.4	0.3
34	TK	209973	-1	-0.9	-0.7	0.91	0.94	0.98	-3.3	-2.2	-2.1	-1.2	-0.9	-0.7	0.573	0.61	0.68	-3.4	-3	-2.8	-2.5	-2.4
35	KD	402541	-0.2	-0.2	-0.2	1.54	1.49	1.4	-1.7	-1.78	-1.8	-0.2	-0.2	-0.2	0.843	0.83	0.828	-0.8	-0.9	-0.98	-0.2	-0.2
36	SD	188308	-0.4	-0.5	-0.5	1.243	1.2	1.17	-1.2	-1.2	-1.3	-0.4	-0.4	-0.3	0.914	0.91	0.98	-1	-1	-0.9	-0.6	-0.8
37	GK	284262	-1.7	-1.6	-1.4	1.085	1.1	1.298	-2.4	-2.2	-2	-1.7	-1.6	-1.4	0.78	0.8	0.87	-1.4	-1.29	-1.21	-1.6	-1.5
38	SS	135439	-2.4	-2.5	-2.6	0.842	0.823	0.789	-2.8	-2.9	-2.9	-2.4	-2.4	-2.6	0.84	0.83	0.825	-3	-3.2	-3.3	-2.6	-2.7
39	GS	184285	1.9	2.1	2.36	1.38	1.452	1.469	-1.3	-1.1	-0.9	1.9	2.1	2.2	0.8	0.898	1.24	-1.6	-1.5	-1	-0.2	-0.1
40	SA	457442	-0.1	-0.1	-0.1	1.052	0.956	0.738	-1.6	-1.7	-1.8	-0.1	-0.1	-0.1	0.998	0.878	0.767	-1.7	-1.8	-1.9	-0.6	-0.7
41	GS	330245	-1.1	-0.9	-0.8	1.004	1.23	1.459	-2.8	-2.5	-2.4	-1.1	-0.9	-0.7	0.71	0.748	0.959	-1.9	-1.5	-1.4	-0.8	-0.7
42	CK	393125	-2.5	-2.6	-2.7	0.62	0.56	0.489	-2	-2.1	-2.3	-2.5	-2.5	-2.7	0.731	0.638	0.539	-0.8	-1	-1.2	1	0.9
43	VK	259465	-1.5	-1.3	-1.2	1.05	1.34	1.45	-2.7	-2.4	-2.2	-1.4	-1.3	-1.2	0.71	0.79	0.938	-2.2	-2	-1.6	-1.7	-1.6
44	AK	405791	1.5	1.6	1.8	1.27	1.32	1.39	-2.6	-2.2	-2	1.5	1.6	1.7	0.73	0.8	0.89	-2.4	-2	-1.9	-1.5	-1.2
45	PK	138774	-0.3	-0.4	-0.5	1.2	1.1	0.938	-0.7	-0.8	-0.9	-0.3	-0.4	-0.5	0.98	0.835	0.689	-1.6	-1.7	-1.8	0.3	0.2
46	PS	250820	0.6	0.8	0.9	1.1	1.35	1	-2.2	-2	-1.8	0.6	0.7	0.9	0.7	0.8	0.9	-0.6	-0.4	-0.2	0.2	0.3
47	BK	236049	-0.7	-0.8	-0.9	0.923	0.905	0.738	-2.9	-3	-3.1	-0.7	-0.8	-0.9	0.698	0.63	0.616	-2.6	-2.8	-2.9	-1.3	-1.5
48	KK	139650	-0.9	-1	-1.2	0.89	0.86	0.852	-2.9	-3	-3.8	-0.9	-1.1	-1.2	0.55	0.509	0.439	-2.6	-2.7	-2.9	-1.2	-1.4
49	NK	211071	-0.1	-0.1	-0.1	1.51	1.43	1.239	-3	-3.1	-3.2	-0.2	-0.1	-0.1	0.672	0.638	0.539	-2.6	-2.8	-2.9	-1.6	-1.8
50	DR	391339	-1.4	-1.7	-1.8	0.78	0.72	0.69	-2.6	-2.8	-2.9	-1.4	-1.5	-1.8	0.67	0.65	0.539	-1	-1.2	-1.3	-0.9	-1.1
51	MD	122053	-2.4	-2.2	-2	1.004	1.189	1.28	-1.8	-1.4	-1.3	-2.4	-2.1	-2	0.832	0.87	0.988	-1.7	-1.6	-1.4	-1.9	-1.7
52	RK	444596	-3.9	-3.8	-3.5	0.813	0.82	0.987	-3.6	-3.4	-3.1	-3.5	-3.3	-3	0.606	0.678	0.789	-3.2	-3	-2.8	-3.3	-3.2
53	BS	134197	-2	-1.8	-1.7	0.83	0.87	0.976	-2.9	-2.6	-2.5	-2	-1.8	-1.6	0.68	0.73	0.89	-2.2	-2.3	-2.1	-1	-0.9
54	SR	215023	-1.6	-1.7	-1.8	0.859	0.821	0.786	-2.5	-2.6	-2.7	-1.6	-1.7	-1.9	0.689	0.59	0.53	-2.1	-2.2	-2.3	-1.4	-1.5
55	RS	297928	1.1	1.2	1.3	1.08	1.123	1.43	-3.2	-3	-2.8	1.1	1.2	1.4	0.593	0.657	0.787	-2.8	-2.5	-2.3	-0.6	-0.4
56	JS	268834	-2	-2.3	-2.3	0.9	0.87	0.823	-2.2	-2.1	-2	-2	-2.2	-2.3	0.8	0.73	0.713	-2.2	-2.1	-2	-1.7	-1.6

S.NO.	Name	MRD	Total hip Z score at 12 months	bone mineral density g/m2 baseline at Total hip	bone mineral density at 6 months at Total hip	bone mineral density at 12 months at Total hip	GI side adverse events due to aleondronate	cardiovascular adverse events due to aleondronate	osteonecrosis due to aleondronate	severe dematological manifestations due to aleondronate	other adverse events due to aleondronate	Hospitalization as an adverse events due to aleondronate	Death as aadverse event due to alondronate	Death	cause of death
1	DS	39091	1.32	0.76	0.75	0.733	NO	NO	NO	NO	NO	NO	NO	NO	NO
2	RS	95232	-0.099	1	1.12	1.13	NO	NO	NO	NO	NO	NO	NO	NO	NO
3	NS	275234	-1.09	0.817	0.715	0.703	NO	NO	NO	NO	NO	NO	NO	NO	NO
4	SA	81489	-0.87	0.876	0.767	0.703	NO	NO	NO	NO	NO	NO	NO	NO	NO
5	NS	358756	-0.4	0.933	0.998	1.1	NO	NO	NO	NO	NO	NO	NO	NO	NO
6	HS	362450	-2.1	0.81	0.88	0.733	YES	NO	NO	NO	NO	NO	NO	NO	NO
7	NJ	146147	-0.9	0.83	0.99	1.2	NO	NO	NO	NO	YES	NO	NO	NO	NO
8	HS	84886	1.326	0.767	0.752	0.713	NO	NO	NO	NO	NO	NO	NO	NO	NO
9	JS	372848	2.6	1.306	1.208	1.007	NO	NO	NO	NO	NO	NO	NO	NO	NO
10	VA	192368	-2	0.584	0.59	0.61	NO	NO	NO	NO	NO	NO	NO	NO	NO
11	HS	189874	-0.29	0.928	0.77	0.717	NO	NO	NO	NO	NO	NO	NO	NO	NO
12	RV	241271	-0.8	0.84	0.72	0.633	NO	NO	NO	NO	NO	NO	NO	NO	NO
13	JG	184776	-2.4	1.324	1.23	1.009	NO	NO	NO	NO	NO	NO	NO	NO	NO
14	RM	197400	-0.6	0.988	0.99	1.1	NO	NO	NO	NO	NO	NO	NO	NO	NO
15	SK	115952	0.723	0.85	0.89	1.009	NO	NO	NO	NO	NO	NO	NO	NO	NO
16	SS	140578	0.89	0.849	0.82	0.733	NO	NO	NO	NO	NO	NO	NO	NO	NO
17	BK	201967	-0.7	0.76	0.89	1.098	NO	NO	NO	NO	NO	NO	NO	NO	NO
18	NK	43405	-0.4	0.912	0.89	0.786	NO	NO	NO	NO	NO	NO	NO	NO	NO
19	GS	198374	0.73	0.68	0.59	0.733	NO	NO	NO	NO	NO	NO	NO	NO	NO
20	SK	371465	-0.7	0.734	0.84	0.97	NO	NO	NO	NO	NO	NO	NO	NO	NO
21	AK	132172	-1.9	0.659	0.79	0.897	NO	NO	NO	NO	NO	NO	NO	YES	Cardiac
22	IS	191015	-1.09	0.772	0.88	0.989	NO	NO	NO	NO	NO	NO	NO	NO	NO
23	RS	451663	-0.3	0.94	0.92	0.83	NO	NO	NO	NO	NO	NO	NO	NO	NO
24	AS	96083	0.3	1.489	1.2	1.19	NO	NO	NO	NO	NO	NO	NO	NO	NO
25	HK	208490	-2.19	0.672	0.79	0.789	NO	NO	NO	YES	NO	NO	NO	NO	NO
26	RC	23008	-1.2	0.821	0.803	0.759	NO	NO	NO	NO	NO	NO	NO	NO	NO
27	RS	182281	-1.4	0.76	0.638	0.598	NO	NO	NO	NO	NO	NO	NO	NO	NO
28	JS	151689	0.5	1.14	1.26	1.48	NO	NO	NO	NO	NO	NO	NO	NO	NO
29	NS	462800	0.2	1.142	1.12	1.107	NO	NO	NO	NO	NO	NO	NO	NO	NO
30	GS	78322	-0.1	1.107	1.15	1.28	NO	NO	NO	NO	NO	NO	NO	NO	NO
31	SP	413783	-0.9	0.682	0.69	0.78	NO	NO	NO	NO	NO	NO	NO	NO	NO
32	PK	415656	-0.9	0.734	0.81	0.987	NO	NO	NO	NO	NO	NO	NO	NO	NO
33	BK	236044	0.299	1.1	0.99	0.975	NO	NO	NO	NO	NO	NO	NO	NO	NO
34	TK	209973	-2.2	0.596	0.61	0.64	NO	NO	NO	NO	NO	NO	NO	NO	NO
35	KD	402541	-0.2	0.98	0.978	0.876	NO	NO	NO	NO	NO	NO	NO	NO	NO
36	SD	188308	-0.9	0.95	0.934	0.923	NO	NO	NO	NO	NO	NO	NO	NO	NO
37	GK	284262	-1.48	0.9	0.99	1.099	YES	NO	NO	NO	NO	NO	NO	NO	NO
38	SS	135439	-2.8	0.627	0.624	0.58	NO	NO	NO	NO	NO	NO	NO	NO	NO
39	GS	184285	-0.1	0.93	0.95	1.114	YES	NO	NO	NO	NO	NO	NO	NO	NO
40	SA	457442	-0.7	0.844	0.82	0.738	NO	NO	NO	NO	NO	NO	NO	YES	Cardiac
41	GS	330245	-0.5	0.823	0.956	1.389	NO	NO	YES	NO	NO	NO	NO	NO	NO
42	CK	393125	0.7	0.935	0.923	0.826	NO	NO	NO	NO	NO	NO	NO	NO	NO
43	VK	259465	-1.5	0.81	0.989	1.25	NO	NO	NO	NO	NO	NO	NO	NO	NO
44	AK	405791	1	0.756	0.9	1.09	NO	NO	NO	NO	NO	NO	NO	NO	NO
45	PK	138774	0.1	1.19	1.004	1.001	NO	NO	NO	NO	NO	NO	NO	NO	NO
46	PS	250820	0.4	1.013	1.34	1.59	NO	NO	NO	NO	NO	NO	NO	NO	NO
47	BK	236049	1.7	0.689	0.567	0.539	NO	NO	NO	NO	NO	NO	NO	NO	NO
48	KK	139650	-1.5	0.66	0.59	0.49	NO	NO	NO	NO	NO	NO	NO	NO	NO
49	NK	211071	-1.9	0.89	0.74	0.67	NO	NO	NO	NO	NO	NO	NO	NO	NO
50	DR	391339	-1.3	0.68	0.63	0.539	NO	NO	NO	NO	NO	NO	NO	NO	NO
51	MD	122053	-1.4	0.785	0.853	0.987	NO	NO	NO	NO	NO	NO	NO	NO	NO
52	RK	444596	-3	0.643	0.678	0.698	NO	NO	NO	NO	NO	NO	NO	NO	NO
53	BS	134197	-0.7	0.74	0.789	0.835	NO	NO	NO	NO	NO	NO	NO	NO	NO
54	SR	215023	-1.7	0.723	0.71	0.638	NO	NO	NO	NO	NO	NO	NO	NO	NO
55	RS	297928	-0.1	0.653	0.752	0.899	NO	NO	NO	NO	NO	NO	NO	NO	NO
56	JS	268834	-1.4	0.75	0.71	0.689	NO	NO	NO	NO	NO	NO	NO	NO	NO

S.NO.	Name	MRD	age	Age group	sex	IPD/ OPD/ HD	Religion	address urban/rural	diagnosis	CKD stage	comorbidity cardiac	comorbidity others	CKD 5D DURATION of dialysis at timeof enrollment in months	Route Hemodialysis/ Peritoneal dialysis	Accees for HD
57	RR	47003	68	4	M	OPD	hindu	rural	Diabetic Nephropathy	5	no	no	0	NAD	NAD
58	BK	59586	70	4	M	OPD	muslim	rural	Diabetic Nephropathy	5	YES LVEF 40%	no	0	NAD	NAD
59	SS	50572	33	1	M	OPD	hindu	urban	Hypertensive Nephrosclerosis	5	no	Hypertension	0	NAD	NAD
60	BJ	343203	51	3	M	OPD	hindu	urban	Diabetic Nephropathy	5	no	no	0	NAD	NAD
61	IS	402328	51	3	M	OPD	hindu	urban	Hypertensive Nephrosclerosis	4	no	no	0	NAD	NAD
62	GG	142664	55	3	M	IDD	hindu	urban	Diabetic Nephropathy	5	YES LVEF 40%	Hypertension	0	NAD	NAD
63	GA	92887	62	4	M	OPD	sikh	urban	Diabetic Nephropathy	4	no	no	0	NAD	NAD
64	KD	402541	61	4	M	OPD	hindu	urban	Hypertensive Nephrosclerosis	4	no	Hypertension	0	NAD	NAD
65	MK	184965	52	3	M	OPD	hindu	urban	Diabetic Nephropathy	4	YES LVEF 38%	Hypertension	0	NAD	NAD
66	MK	81461	59	3	M	OPD	hindu	urban	Diabetic Nephropathy	4	no	no	0	NAD	NAD
67	SS	408762	48	2	F	OPD	hindu	urban	Hypertensive Nephrosclerosis	4	no	Hypertension	0	NAD	NAD
68	SB	397124	64	4	F	OPD	sikh	urban	Hypertensive Nephrosclerosis	4	no	Hypertension	0	NAD	NAD
69	JS	348337	49	2	F	OPD	hindu	rural	Diabetic Nephropathy	4	no	Hypertension	0	NAD	NAD
70	BN	378821	31	1	M	OPD	hindu	urban	Diabetic Nephropathy	3	no	no	0	NAD	NAD
71	JS	92335	52	3	F	OPD	sikh	urban	Hypertensive Nephrosclerosis	3	no	Hypertension,Rheumatoid Arthritis	0	NAD	NAD
72	DK	228268	70	4	F	OPD	sikh	urban	Hypertensive Nephrosclerosis	3	no	Hypertension	0	NAD	NAD
73	KS	413725	70	4	M	IPD	sikh	urban	Diabetic Nephropathy	3	no	Alcohalic CLD	0	NAD	NAD
74	PK	26543	56	3	M	OPD	hindu	urban	Diabetic Nephropathy	3	no	no	0	NAD	NAD
75	GK	465450	48	2	F	OPD	muslim	urban	Diabetic Nephropathy	3	no	no	0	NAD	NAD
76	DS	329217	39	1	M	OPD	hindu	urban	Hypertensive Nephrosclerosis	3	no	Hypertension	0	NAD	NAD
77	NK	185818	58	3	M	OPD	hindu	urban	Diabetic Nephropathy	3	no	Hypertension	0	NAD	NAD
78	SJ	50140	70	4	F	OPD	sikh	urban	ADPKD	3	no	no	0	NAD	NAD
79	PN	479738	63	4	M	OPD	sikh	rural	Diabetic Nephropathy	3	no	no	0	NAD	NAD
80	US	485017	49	2	M	OPD	sikh	rural	Diabetic Nephropathy	3	no	no	0	NAD	NAD

S.NO.	Name	MRD	frequency per week	Aleondronate given by oral route	compliance to alondronate	erythropoietin therapy	weight in Kg	Height in cm	SBP	DBP	pallor	Skin manifestation	Hemoglobin baseline g/dl	Hemoglobin at 3 month	Hemoglobin at 6 months	Hemoglobin at 12 months	TLC baseline per ul	TLC at 3 months	TLC at 6 months	TLC at 12 months
57	RR	47003	0	No	good	yes	58	163	132	82	yes	yes	10.4	9.7	9.3	9.8	10	5.4	10.4	10.4
58	BK	59586	0	No	NAD	yes	63	165	128	86	yes	yes	8.9	9.2	9.1	9.7	10.4	8.2	8.3	8.1
59	SS	50572	0	yes	good	yes	66	167	130	80	yes	no	9.2	9.3	9.4	9.8	9.3	10.2	8.1	10.4
60	BJ	343203	0	No	NAD	yes	67	168	132	80	yes	no	9.1	9.2	9.5	9.6	5.4	10.4	9.3	10
61	IS	402328	0	No	NAD	yes	59	166	130	80	yes	no	8.8	9.6	9.5	10.2	8.2	10	5.4	10.4
62	GG	142664	0	yes	good	yes	63	171	120	80	yes	no	9.4	9.2	9.6	10	11.2	10.4	8.2	8.3
63	GA	92887	0	No	NAD	yes	62	169	130	80	yes	no	10.4	9.7	9.3	9.8	10.8	8.3	7.3	8.1
64	KD	402541	0	yes	good	yes	65	168	132	80	yes	no	8.9	9.2	9.1	9.7	11.2	7.3	10.6	7.6
65	MK	184965	0	No	NAD	yes	71	169	124	80	yes	no	9.4	9.2	9.6	10	6.9	6.3	10.2	7.2
66	MK	81461	0	yes	good	yes	77	168	138	80	yes	no	10.4	9.7	9.3	9.8	9.3	7.3	10.6	5.3
67	SS	408762	0	No	NAD	yes	73	166	130	90	yes	no	8.9	9.2	9.1	9.7	7.7	6.3	10.2	10.3
68	SB	397124	0	yes	good	yes	52	167	130	80	yes	no	9.2	9.3	9.4	9.8	7.2	7.7	10.3	9.7
69	JS	348337	0	yes	good	yes	61	170	134	86	yes	yes	9.1	9.5	9.1	10.2	6.6	7.2	10.2	9.3
70	BN	378821	0	yes	good	yes	64	168	130	78	yes	yes	8.9	9.2	9.3	9.9	7.7	6.6	10.4	10.4
71	JS	92335	0	yes	good	yes	63	167	120	90	yes	yes	8.7	9.2	9.1	9.8	9.3	7.7	8.3	7.3
72	DK	228268	0	No	NAD	yes	59	168	130	80	yes	yes	8.8	9.6	9.5	10.2	10.4	7.2	8.1	6.3
73	KS	413725	0	yes	good	yes	57	166	132	84	yes	yes	9.4	9.2	9.6	10	8.1	6.6	7.3	7.4
74	PK	26543	0	No	NAD	yes	64	159	120	70	yes	yes	10.4	9.7	9.3	9.8	9.3	7.7	6.6	8.3
75	GK	465450	0	yes	good	yes	65	167	110	78	yes	yes	8.9	9.2	9.1	9.7	5.4	7.6	7.7	8.1
76	DS	329217	0	No	NAD	yes	59	168	132	82	yes	no	9.2	9.3	9.4	9.8	8.2	7.2	7.2	9.3
77	NK	185818	0	yes	good	yes	55	166	128	86	yes	no	9.1	9.2	9.5	9.6	7.3	11.2	6.6	5.4
78	SJ	50140	0	No	NAD	yes	57	171	134	90	yes	no	11.2	9.4	9.8	10	6.6	11.2	8.1	8.2
79	PN	479738	0	yes	good	yes	59	169	120	70	yes	no	10.2	9.2	9.7	9.8	10.4	7.3	9.3	7.3
80	US	485017	0	No	NAD	yes	71	168	124	86	yes	no	8.8	9.3	9.5	9.9	9.3	7.8	5.4	10.6

S.NO.	Name	MRD	Platelets at baseline lakh	Platelets at 3 months	Platelets at 6 months	Platelets at 12 months	ESR at baseline mm/first hr	Urea at baseline mg/dl	Urea at 3 months	Urea at 6 months	Urea at 12 months	CREATININE baseline mg/dl	Creatinine at 3 months	creatinine at 6 months	creatinine at 12 months	sodium baseline meq/l	sodium at 3 months	sodium at 6 months	sodium at 12 months	potassium at baseline meq/l	potassium at 3 months
57	RR	47003	1.43	1.34	1.43	1.34	30	157	98	139	145	4.4	5.9	6.2	6.3	135	138	133	135	5.4	3.3
58	BK	59586	1.39	1.33	1.39	2.1	27	119	98	116	142	5.9	5.9	5.9	6.2	130	137	136	130	4.2	3.7
59	SS	50572	1.63	1.34	1.46	1.5	17	132	139	157	128	4	4.1	4.1	4.2	137	136	130	141	5.8	4.7
60	BJ	343203	1.84	1.46	1.24	1.34	29	135	116	119	137	4.8	4.9	4.9	5.1	137	136	130	132	3.2	3.6
61	IS	402328	1.84	1.43	1.34	1.46	17	139	134	115	119	4.2	4.2	4.2	4.7	124	133	141	147	5.3	3.6
62	GG	142664	1.39	1.63	1.66	1.63	20	116	129	121	132	5.9	5.9	5.9	6.9	143	138	132	136	5.4	4.9
63	GA	92887	1.34	1.24	1.46	1.24	23	157	116	116	132	3.6	3.6	3.7	3.9	135	138	147	133	4.2	4.2
64	KD	402541	2.1	1.34	1.43	1.34	22	119	157	157	98	3.8	3.9	3.9	4	132	133	119	138	2.2	3.8
65	MK	184965	1.46	1.33	1.39	2.1	17	132	142	145	142	4.2	4.2	4.2	4.3	147	138	127	138	6.2	5.4
66	MK	81461	1.43	1.98	1.64	1.57	15	135	128	145	157	4.1	4.2	4.7	4.9	133	138	152	137	5.4	5.8
67	SS	408762	1.39	1.8	1.5	1.9	21	145	139	115	119	3.5	3.9	3.9	4.2	136	137	129	124	3.2	4.3
68	SB	397124	1.64	1.9	1.34	2.13	17	142	156	121	132	2.9	2.9	2.9	3.4	143	141	133	143	5.8	4.8
69	JS	348337	1.5	1.42	1.34	1.24	23	128	116	116	132	3.1	3.1	3.2	3.3	135	132	144	133	3.2	5.4
70	BN	378821	1.64	1.63	1.34	1.63	17	139	157	157	98	1.8	1.9	2	2.3	124	133	122	135	5.3	3.3
71	JS	92335	1.46	1.45	1.26	1.24	30	156	119	119	98	1.9	1.9	2	2.1	143	138	119	139	5.4	3.6
72	DK	228268	1.43	1.84	1.43	1.34	27	132	139	132	139	1.9	1.9	2.2	2.2	129	141	149	133	3.3	3.7
73	KS	413725	2.1	1.39	1.63	2.1	17	98	116	135	116	1.9	2	2	2.3	135	138	137	138	3.7	4.1
74	PK	26543	1.5	1.46	1.24	1.46	29	98	134	139	134	1.7	1.8	1.9	1.9	130	137	124	137	4.7	5.3
75	GK	465450	1.34	1.43	1.34	1.43	17	139	115	119	139	1.8	1.8	1.9	1.9	133	132	135	124	3.6	4.4
76	DS	329217	1.46	1.39	1.33	1.39	17	116	121	132	116	1.8	1.9	2	2.3	138	147	124	143	3.3	3.2
77	NK	185818	1.63	1.63	1.34	1.63	23	134	116	132	119	1.7	1.9	2.1	2.2	138	133	135	135	3.6	4.8
78	SJ	50140	1.24	1.84	1.46	1.24	17	129	157	98	139	1.7	1.8	1.7	1.7	137	136	130	130	3.7	5.4
79	PN	479738	1.34	1.33	1.33	1.34	30	116	117	131	123	1.9	1.9	2	2.1	136	130	141	133	4.1	4.2
80	US	485017	1.98	1.64	1.57	1.79	27	119	123	134	117	2.1	2.1	2.3	2.3	136	130	132	138	5.3	5.7

S.NO.	Name	MRD	potassium at 6 months	potassium at 12 months	Calcium baseline mg/dl	calcium at 3 months	calcium at 6 months	calcium at 12 months	phosphorus mg/dl baseline	phosphorus at 3 months	phosphorus at 6 months	phosphorus at 12 months	alakaline phosphotase base line U/dl	alkaline phosphatase at 3 months	alkaline phosphatase at 6 months	alkaline phosphatase at 12 months	Uric acid baseline mg/dl	uric acid at 3 months	uric acid at 6 months	uric acid at 12 months	Total protein mg/dl baseline
57	RR	47003	3.6	4.9	8.1	8.9	8.3	9.4	6.6	6.6	5.6	6.5	144	130	165	144	7.6	6.8	8.6	9.1	6.5
58	BK	59586	5.2	4.2	8.3	8.6	8.5	7.8	6.5	6.4	6.8	6.8	162	154	139	137	6.8	6.6	5.6	8.6	6.7
59	SS	50572	6.1	5.7	8.1	8.7	8.4	7.9	5.6	8.6	6.2	5.6	137	137	165	164	6.7	6.9	7.6	8.3	6.9
60	BJ	343203	6.3	5.4	9.4	8.6	10.1	8.3	7.6	5.6	6.2	6.4	162	130	139	144	9.1	8.6	8.3	8.8	5.7
61	IS	402328	6	3.2	9.6	8.5	8.6	8.4	6.8	7.6	5.6	6.2	168	154	146	162	8.6	9.3	8.5	9.6	6.7
62	GG	142664	5.4	5.8	8.6	7.9	8.4	8.3	6.2	6.2	7.6	5.9	146	164	139	137	8.3	7.8	8.4	8.6	6.8
63	GA	92887	3.3	4.3	8.4	8.3	8.8	8.6	6.2	6.6	6.2	6.8	139	159	144	162	8.8	8.3	8.3	8.4	5.9
64	KD	402541	4.2	3.6	8.8	8.5	9.3	8.3	5.6	6.5	5.9	6.4	144	162	137	148	9.6	8.5	8.6	8.8	6.9
65	MK	184965	5.8	3.7	9.3	8.4	7.8	8.7	8.6	5.6	5.6	6.8	137	137	130	146	8.6	8.4	7.9	9.3	6.5
66	MK	81461	5.3	5.7	7.8	8.3	8.3	7.9	10.6	6.1	6.8	8.6	130	165	157	139	8.4	8.3	9.9	8.5	6.9
67	SS	408762	5.4	5.4	10.1	8.6	8.5	8.6	7.6	6.7	6.2	5.6	165	139	165	144	8.8	8.6	8.7	8.4	5.9
68	SB	397124	4.2	3.2	7.1	8.8	8.4	8.5	6.2	7.2	6.2	7.6	139	146	139	132	9.3	8.3	7.9	8.3	6.9
69	JS	348337	2.2	5.8	8.9	8.4	10.1	7.9	5.9	6.2	5.6	6.2	146	139	147	130	6.6	6.8	6.6	8.6	6.6
70	BN	378821	6.2	3.2	10.1	9.9	7.1	8.3	7.6	5.6	8.6	5.6	156	144	157	165	6.5	6.7	6.9	8.6	6.8
71	JS	92335	5.7	3.3	7.1	9.2	8.9	7.9	6.2	7.6	10.6	9.8	144	157	165	139	6.2	6.6	6.6	8.4	6.6
72	DK	228268	5.4	4.7	8.5	8.6	10.1	8.4	5.9	6.4	7.5	7.9	130	137	159	146	6.8	6.5	6.4	8.8	6.8
73	KS	413725	3.2	3.6	8.4	7.9	7.1	8.3	5.6	6.8	6.5	5.6	165	130	162	156	6.6	5.6	8.6	9.3	6.7
74	PK	26543	5.8	3.6	8.3	9.9	8.9	8.6	7.6	6.6	5.6	6.2	139	157	160	144	6.5	7.6	5.6	7.8	5.2
75	GK	465450	4.2	4.9	8.6	8.7	9.4	8.3	6.2	6.5	7.6	6.6	146	165	162	165	5.6	6.2	7.6	5.8	6.2
76	DS	329217	2.2	4.2	8.3	7.9	8.6	8.7	5.9	5.6	6.2	6.5	156	139	160	139	7.6	5.9	6.2	6.8	6.3
77	NK	185818	6.2	5.7	8.3	9.9	8.1	7.8	6.8	7.6	5.9	5.6	144	147	146	146	6.2	6.8	5.6	6.6	6.5
78	SJ	50140	5.7	5.4	8.6	8.7	9.1	9.4	6.2	6.2	6.8	7.6	137	157	139	139	6.6	5.6	8.6	6.9	6.7
79	PN	479738	5.4	5.4	8.3	7.9	8.6	10.9	6.2	6.6	5.6	6.2	139	146	139	144	6.6	6.6	6.7	6.9	6.9
80	US	485017	3.2	5.8	7.8	8.7	8.6	10.7	5.6	6.5	7.6	5.9	146	139	147	157	6.2	6.8	5.6	6.8	5.7

S.NO.	Name	MRD	Total protein at 3 months	Total protein at 6 months	Total protein at 12 months	Albumin mg/dl baseline	Albumin at 3 months	Albumin at 6 months	Albumin at 12 months	SGOT U/L baseline	SGOT at 3 months	SGOT at 6 months	SGOT at 12 months	SGPT U/L baseline	SGPT at 3 months	SGPT at 6 months	SGPT at 12 months	Total bilirubin mg/dl baseline	Total bilirubin at 3 months	Total bilirubin at 6 months	Total bilirubin at 12 months	IPTH pg/ml baseline	iPTH at 3 months	iPTH at 6 months
57	RR	47003	6.7	6.8	6.9	3.1	3.5	3.1	3.7	16	22	23	24	21	16	19	22	0.9	0.8	0.6	0.5	207	213	213
58	BK	59586	6.8	6.7	6.6	3.5	3.5	3.5	3.8	21	21	19	21	22	21	16	21	0.7	0.9	0.9	0.4	210	169	192
59	SS	50572	6.7	6.9	6.8	3.4	3.7	3.2	3.7	22	28	24	22	21	22	21	28	0.8	0.7	0.4	0.6	198	178	172
60	BJ	343203	6.6	6.9	6.7	3.3	3.4	3.8	3.4	21	21	21	21	28	21	22	24	0.5	0.6	0.5	0.9	202	205	187
61	IS	402328	6.8	6.5	6.8	3.5	3.5	3.7	3.1	28	20	22	28	24	28	21	21	0.4	0.9	0.5	0.7	187	192	197
62	GG	142664	6.7	6.9	6.7	3.7	3.5	3.7	3.5	21	21	21	24	21	21	21	21	0.7	0.5	0.4	0.6	198	205	193
63	GA	92887	6.8	5.9	6.8	3.4	3.8	3.8	3.9	21	21	23	21	23	21	23	22	0.6	0.3	0.7	0.8	207	190	180
64	KD	402541	6.7	6.5	6.7	3.5	3.7	3.7	3.9	16	28	21	21	21	20	19	21	0.9	0.8	0.6	0.5	210	194	190
65	MK	184965	6.8	6.8	6.6	3.2	3.4	3.4	3.7	21	21	21	20	20	21	18	28	0.7	0.9	0.9	0.4	205	194	176
66	MK	81461	6.7	6.7	6.8	3.8	3.5	3.8	3.7	22	23	20	21	21	18	22	21	0.6	0.7	0.7	0.7	190	189	192
67	SS	408762	6.8	6.9	6.7	3.7	3.9	3.7	3.8	21	19	21	18	18	19	21	23	0.8	0.6	0.6	0.6	215	205	204
68	SB	397124	5.2	6.9	6.8	3.4	3.7	3.4	3.7	28	24	22	19	19	16	23	19	0.5	0.8	0.8	0.8	198	192	207
69	JS	348337	6.2	6.5	6.7	3.5	3.8	3.5	3.1	21	21	19	16	16	21	19	24	0.4	0.5	0.5	0.8	215	205	210
70	BN	378821	6.3	6.9	6.6	3.4	3.7	3.2	3.7	20	22	21	21	21	22	16	21	0.7	0.4	0.4	0.8	198	192	198
71	JS	92335	6.2	5.9	6.8	3.3	3.4	3.8	3.4	21	21	21	22	22	21	21	22	0.6	0.7	0.7	0.9	211	212	202
72	DK	228268	6.3	6.7	6.2	3.7	3.1	3.4	3.7	18	28	22	21	21	28	22	21	0.9	0.8	0.6	0.5	190	178	187
73	KS	413725	6.5	6.8	6.3	3.4	3.4	3.9	3.8	19	24	21	28	28	21	21	28	0.7	0.9	0.9	0.4	198	192	198
74	PK	26543	6.8	6.6	6.2	3.1	3.5	3.9	3.7	16	21	28	21	21	22	28	24	0.6	0.7	0.7	0.7	197	192	207
75	GK	465450	6.9	6.8	6.3	3.4	3.5	3.7	3.5	21	20	21	23	23	21	21	21	0.8	0.6	0.6	0.6	206	205	210
76	DS	329217	6.8	6.7	6.5	3.5	3.9	3.8	3.7	22	21	23	19	19	21	23	23	0.5	0.8	0.8	0.8	205	192	198
77	NK	185818	6.7	6.8	6.8	3.5	3.7	3.7	3.8	19	18	19	16	16	23	19	19	0.4	0.5	0.5	0.8	205	210	169
78	SJ	50140	6.1	6.6	6.6	3.5	3.8	3.4	3.7	22	28	24	18	19	19	19	25	0.7	0.4	0.4	0.8	192	198	178
79	PN	479738	5.2	6.8	6.8	3.8	3.1	3.5	3.1	21	21	21	19	16	16	16	25	0.6	0.7	0.7	0.9	200	202	205
80	US	485017	6.2	6.5	6.9	3.7	3.4	3.7	3.4	28	20	22	16	21	21	21	25	0.9	0.6	0.6	0.7	178	187	192

S.NO.	Name	MRD	iPTH at 12 months	vitamin D3 ng/ml baseline	vitamin D3 at 3 months	vitamin D3 at 6 months	vitamin D3 at 12 months	Fracture at Xray DL spine at baseline	Fracture at Xray DL spine at 12 months	Fracture at Xray DL spine at 12 months	fracture in chest X ray at baseline	fracture in chest X ray at 6 months	fracture in chest X ray at 12 months	fracture in X ray hand at baseline	fracture in X ray hand at 6 months	fracture in X ray hand at 12 months	subperiosteal resorbtion of phalanges on x ray hand	calcification of abdominal aorta on x ray of lumbar spine	lumbar spine T score baseline	lumbar spine T score 6 months	lumbar spine T score 12 months
57	RR	47003	198	26	30	23	28	no	no	no	no	no	no	no	no	no	NO	NO	-1.6	-1.5	-1.4
58	BK	59586	189	26	23	22	30	no	no	no	no	no	no	no	no	no	NO	NO	1.3	1.2	1
59	SS	50572	167	24	28	28	31	no	no	no	no	no	no	no	no	no	NO	NO	0.1	0.2	0.4
60	BJ	343203	178	25	26	22	28	no	no	no	no	no	no	no	no	no	NO	NO	-2	-2.1	-2.3
61	IS	402328	180	27	25	28	26	no	no	no	no	no	no	no	no	no	NO	NO	-2.1	-2.1	-2.2
62	GG	142664	178	30	27	30	26	no	no	no	no	no	no	no	no	no	NO	NO	-1.4	-1.3	-1.2
63	GA	92887	165	23	30	31	24	no	no	no	no	no	no	no	no	no	NO	NO	-2.2	-2.1	-2
64	KD	402541	172	22	23	28	25	no	no	no	no	no	no	no	no	no	NO	NO	-2.9	-2.8	-2.4
65	MK	184965	178	28	22	26	27	no	no	no	no	no	no	no	no	no	NO	NO	-0.4	-0.6	-0.8
66	MK	81461	175	22	28	26	30	no	no	no	no	no	no	no	no	no	NO	NO	-1.8	-1.5	-1.4
67	SS	408762	198	26	22	24	23	no	no	no	no	no	no	no	no	no	NO	NO	1.9	1.8	1.5
68	SB	397124	190	26	27	25	22	no	no	no	no	no	no	no	no	no	NO	NO	-3	-2.7	-2.3
69	JS	348337	169	24	26	27	28	no	no	no	no	no	no	no	no	no	NO	NO	0.1	0.1	0.2
70	BN	378821	178	26	22	24	22	no	no	no	no	no	no	no	no	no	NO	NO	1.2	1.3	0.4
71	JS	92335	196	26	27	25	27	no	no	no	no	no	no	no	no	no	NO	NO	-1.2	-1.1	-1
72	DK	228268	192	24	26	27	26	no	no	no	no	no	no	no	no	no	NO	NO	-2.1	-2.2	-2.4
73	KS	413725	188	25	22	30	22	no	no	no	no	no	no	no	no	no	NO	NO	-1.7	-1.5	-1.3
74	PK	26543	190	27	23	26	23	no	no	no	no	no	no	no	no	no	NO	NO	-1.3	-1.4	-1.4
75	GK	465450	194	30	26	26	26	no	no	no	no	no	no	no	no	no	NO	NO	-1.6	-1.4	-1.2
76	DS	329217	178	23	24	24	24	no	no	no	no	no	no	no	no	no	NO	NO	-2	-2.1	-2.2
77	NK	185818	165	22	25	25	25	no	no	no	no	no	no	no	no	no	NO	NO	-1.6	-1.5	-1.2
78	SJ	50140	170	28	27	27	27	no	no	no	no	no	no	no	no	no	NO	NO	-1.7	-1.9	-2
79	PN	479738	179	22	30	30	30	no	no	no	no	no	no	no	no	no	NO	NO	0.5	0.7	0.9
80	US	485017	189	27	23	23	22	no	no	no	no	no	no	no	no	no	NO	NO	-1.7	-1.7	-1.9

S.NO.	Name	MRD	lumbar spine Z score baseline	lumbar spine Z score at 6 months	lumbar spine Z score at 12 months	Lumbar spine Bone mineral density baseline g/m2	Lumbar spine Bone mineral density at 6 months	Lumbar spine Bone mineral density at 12months	femur neck T score baseline	femur neck T score at 6 months	femur neck T score at 12 months	femur neck Z score baseline	femur neck Z score at 6 months	femur neck Z score at 12 months	bone mineral density g/m2 baseline at femur neck	bone mineral density at 6 months at femur neck	bone mineral density 12 months at femur neck	Total hip T score at baseline	Total hip T score at 6 months	Total hip T score at 12 months	Total hip Z score at baseline	Total hip Z score at 6 months
57	RR	47003	-0.8	-0.7	-0.5	0.821	0.89	0.928	-1.7	-1.4	-1.2	-0.8	-0.6	-0.5	0.629	0.732	0.835	-2.5	-2.3	-2	-1	-0.9
58	BK	59586	0.6	0.5	0.4	1.56	1.52	1.5	-1.5	-1.6	-1.7	0.6	0.5	0.3	0.95	0.92	0.89	0.2	0.1	0.1	-1	-0.9
59	SS	50572	0.21	0.3	0.5	1.244	1.38	1.567	-1.6	-1.5	-1.2	0.3	0.3	0.5	1.086	1.18	1.32	0.4	0.5	0.7	0.5	0.5
60	BJ	343203	-1.6	-1.7	-1.8	0.98	0.954	0.945	-1.8	-2	-2.2	-1.6	-1.6	-1.8	0.78	0.72	0.689	-1.4	-1.5	-1.6	-1.1	-0.9
61	IS	402328	-2.2	-2.2	-2.4	0.969	0.89	0.78	-0.5	-0.5	-0.6	-2.2	-2.3	-2.4	1.04	0.9	0.82	-0.6	-0.7	-0.7	-0.5	-0.5
62	GG	142664	-0.7	-0.5	-0.4	1.052	1.08	1.28	-2	-1.8	-1.5	-0.7	-0.6	-0.4	0.815	0.88	0.9	-1.5	-1.4	-1.2	-0.8	-0.6
63	GA	92887	1.8	1.7	1.7	1.7	1.689	1.6	-0.7	-0.6	-0.5	1.8	1.7	1.6	0.97	0.93	0.878	0.2	0.1	0.1	0.9	0.8
64	KD	402541	-1.5	-1.4	-1.2	0.84	0.87	0.98	-2.6	-2.5	-2.4	-1.5	-1.3	-1.2	0.673	0.73	0.87	-2.4	-2.3	-2.2	-0.8	-0.7
65	MK	184965	-0.1	-0.1	-0.1	1.16	1.1	1.046	-1.1	-1.5	-1.6	-0.1	-0.1	-0.1	0.879	0.7	0.687	-1.6	-1.6	-1.7	-0.5	-0.5
66	MK	81461	-0.7	-0.5	-0.4	1.052	1.09	1.2	-1.7	-1.5	-1.4	-0.7	-0.6	-0.4	0.681	0.71	0.85	-2.3	-2.2	-2	-1.6	-1.3
67	SS	408762	1.9	1.8	1.7	1.403	1.38	1.29	-1.2	-1.4	-1.5	1.9	1.8	1.5	0.89	0.83	0.73	-0.8	-0.9	-0.9	-0.6	-0.7
68	SB	397124	0.3	0.4	0.7	0.909	0.91	0.989	-1.8	-1.7	-1.6	0.3	0.4	0.6	0.817	0.85	0.91	-0.9	-0.5	-0.3	1.2	1.5
69	JS	348337	-0.7	-0.6	-0.5	1.2	1.29	1.39	-0.9	-0.8	-0.7	-0.7	-0.6	-0.4	0.944	1.089	1.345	0.9	1.3	1.56	-0.4	-0.3
70	BN	378821	0.5	0.6	0.8	0.829	0.986	1.23	-1.5	-1.3	-1.2	0.5	0.6	0.7	0.834	0.898	1.34	-1.6	-1.4	-1.3	0.2	0.3
71	JS	92335	-0.4	-0.2	-0.2	1.043	1.2	1.29	-2.2	-2	-1.8	-0.4	-0.2	-0.1	0.743	0.79	0.889	-1.9	-1.7	-1.5	-0.6	-0.4
72	DK	228268	-0.1	-0.1	-0.1	0.923	0.9003	0.897	-0.5	-0.5	-0.6	-0.1	-0.1	-0.2	0.94	0.83	0.74	-2	-2.1	-2.3	-0.2	-0.3
73	KS	413725	-0.7	-0.5	-0.4	0.74	0.8	0.98	-1.6	-1.5	-1.2	-0.7	-0.6	-0.4	1.056	1.078	1.379	-1.5	-1.4	-1.2	-0.3	-0.2
74	PK	26543	-0.1	-0.1	-0.2	1.1	1.09	0.968	-2	-2.1	-2.2	-0.1	-0.1	-0.2	1.32	1.27	1.18	-2	-2.2	-2.3	-0.2	-0.3
75	GK	465450	0.1	0.3	0.4	1.19	1.27	1.38	-0.9	-0.6	-0.5	0.1	0.2	0.4	0.94	0.98	1.124	-2.2	-2	-1.9	-0.3	-0.2
76	DS	329217	-1.4	-1.5	-1.7	1.028	0.987	0.876	-1.5	-1.6	-1.8	-1.4	-1.5	-1.7	0.89	0.789	0.687	-2	-2.2	-2.3	-0.4	-0.5
77	NK	185818	-0.1	-0.1	-0.1	1.12	1.32	1.435	-1.6	-1.5	-1	-0.1	-0.1	-0.1	0.989	1.12	1.38	-2	-1.7	-1.5	-0.7	-0.5
78	SJ	50140	-0.4	-0.5	-0.7	1.12	1.09	0.897	-1.7	-1.8	-1.9	-0.4	-0.4	-0.7	1.23	1.134	1.023	-1.7	-1.5	-1.3	-0.5	-0.3
79	PN	479738	1.1	1.3	1.5	1.23	1.43	1.538	-1.7	-1.5	-1.2	1.1	1.2	1.5	1.13	1.34	1.59	0.7	0.9	1	0.3	0.4
80	US	485017	-0.4	-0.5	-0.7	1.123	1.089	0.987	-1.5	-1.6	-1.7	-0.3	-0.5	-0.7	1.23	1.14	1.098	0.5	0.3	0.2	-1.5	-1.6

S.NO.	Name	MRD	Total hip Z score at 12 months	bone mineral density g/m2 baseline at Total hip	bone mineral density at 6 months at Total hip	bone mineral density at 12 months at Total hip	GI side adverse events due to aleondronate	cardiovascular adverse events due to aleondronate	osteonecrosis due to aleondronate	severe dematological manifestations due to aleondronate	other adverse events due to aleondronate	Hospitalization as an adverse events due to aleondronate	Death as aadverse event due to alondronate	Death	cause of death
57	RR	47003	-0.8	0.69	0.71	0.89	NO	NO	NO	NO	NO	NO	NO	NO	NO
58	BK	59586	-0.7	1.13	1.089	1.068	NO	NO	NO	NO	NO	NO	NO	NO	NO
59	SS	50572	0.7	1.14	1.57	1.638	NO	NO	NO	NO	NO	NO	NO	NO	NO
60	BJ	343203	-0.7	0.89	0.867	0.79	NO	NO	NO	NO	NO	NO	NO	NO	NO
61	IS	402328	-0.4	1.34	1.23	1.19	NO	NO	NO	NO	NO	NO	NO	NO	NO
62	GG	142664	-0.4	0.59	0.76	0.884	NO	NO	NO	NO	NO	NO	NO	NO	NO
63	GA	92887	0.7	1.2	1.114	1.21	NO	NO	NO	NO	NO	NO	NO	NO	NO
64	KD	402541	-0.5	0.732	0.78	0.89	NO	NO	NO	NO	NO	NO	NO	NO	NO
65	MK	184965	-0.4	1	1.01	0.92	NO	NO	NO	NO	NO	NO	NO	YES	Cardiac
66	MK	81461	-1.2	0.771	0.89	0.95	NO	NO	NO	NO	NO	NO	NO	NO	NO
67	SS	408762	-0.8	0.986	0.932	0.901	NO	NO	NO	NO	NO	NO	NO	NO	NO
68	SB	397124	1.8	0.971	1.184	1.345	NO	NO	NO	NO	NO	NO	NO	NO	NO
69	JS	348337	-0.2	1	1.012	1.23	NO	NO	NO	NO	NO	NO	NO	NO	NO
70	BN	378821	0.5	0.834	1.23	1.45	NO	NO	NO	NO	NO	NO	NO	NO	NO
71	JS	92335	-0.2	0.705	0.798	0.879	YES	NO	NO	NO	NO	NO	NO	NO	NO
72	DK	228268	-0.5	0.91	0.87	0.789	NO	NO	NO	NO	NO	NO	NO	NO	NO
73	KS	413725	-0.1	1.23	1.345	1.549	NO	NO	NO	NO	NO	NO	NO	NO	NO
74	PK	26543	-0.5	1.45	1.32	1.189	NO	NO	NO	NO	NO	NO	NO	NO	NO
75	GK	465450	-0.1	0.956	1.23	1.358	NO	NO	NO	NO	NO	NO	NO	NO	NO
76	DS	329217	-0.7	1.02	1.001	0.967	NO	NO	NO	NO	NO	NO	NO	NO	NO
77	NK	185818	-0.4	1.034	1.23	1.348	YES	NO	NO	NO	NO	NO	NO	NO	NO
78	SJ	50140	-0.2	1.23	1.12	1.023	NO	NO	NO	NO	NO	NO	NO	NO	NO
79	PN	479738	0.5	1.34	1.45	1.538	NO	NO	NO	NO	NO	NO	NO	NO	NO
80	US	485017	-1.7	1.23	1.12	0.98	NO	NO	NO	NO	NO	NO	NO	NO	NO

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The Principal
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Subject: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 31.08.2018 has approved the plan of thesis of Sachin Mehra, a student of your college for DM Nephrology along with the names of Supervisor/Co-Supervisors as under:

Topic Plan of Thesis
To study the prevalence of osteoporosis and the efficacy and safety of antiresorptive therapy in CKD(3-5D patients

Supervisor
Dr. Vikas Makkar
Prof. & Head,
Dept. of Nephrology,
DMCH, Ludhiana.

Co-Supervisor
Dr. Parminder Singh
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The student has to submit the four copies of thesis, to the Controller of Examinations, BFUHS, Faridkot at least six months before the commencement of theory examination, to enable to otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the University form while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-supervisor/change of topics if any)

Dr. S P Singh MS(Opth)
Controller of Examinations

Note :
1. (Faculty please note) Thesis registration application to Supervisor/Co-Supervisor, duly signed by the candidate should be submitted to the office of the Controller of Examinations at least 30 days before the commencement of theory examination.
2. The candidate may submit the thesis as per the schedule mentioned above but not later than 31st May of the year of examination. In the event of candidate failing to submit the thesis by 31st May of the year of examination, the candidate will be required to pay the fee for the next year of examination.

TO STUDY THE PREVALENCE OF OSTEOPOROSIS AND THE EFFICACY AND SAFETY OF ANTIRESORPTIVE THERAPY IN CKD3-5D PATIENTS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DM

IN

NEPHROLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

FEBRUARY 2018

DR. SUDHIR MEHTA

DEPARTMENT OF NEPHROLOGY
DAYANAND MEDICAL COLLEGE & HOSPITAL,
LUDHIANA

ABSTRACT OF PLAN OF THESIS

TITLE	**TO STUDY THE PREVALENCE OF OSTEOPOROSIS AND THE EFFICACY AND SAFETY OF ANTIRESORPTIVE THERAPY IN CKD3-5D PATIENTS**
For Degree of	DM NEPHROLOGY
Candidate	**Dr. Sudhir Mehta**
Supervisor	**Dr. Vikas Makkar,** Professor and Head Department of Nephrology, Dayanand Medical College and Hospital, Ludhiana
Co- Supervisor	**Dr. Parminder Singh,** Professor and Head Department of Endocrinology, Dayanand Medical College and Hospital Ludhiana
Co- Supervisor	**Dr. Preet Mohinder Singh**, Assistant Professor Department of NEPHROLOGY, Dayanand Medical College and Hospital, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences Faridkot

Introduction: Changes in bone and mineral metabolism occur early in the course of CKD. The prevalence of low bone mineral density (BMD) and osteoporosis increases with greater seventy of chronic kidney disease (CKD). So this study was done to study the efficacy and safety of Antiresorptive therapy in CKD3-5D patients and to study the prevalence of osteoporosis in patients with CKD3-5D.

Aims & objectives:(1) To study the prevalence of osteoporosis in CKD 3-5D patients. (2) To study the effect of antiresorptive therapy on bone mineral density (BMD) in CKD 3-5D patients, (3) To assess the adverse reactions of antiresorptive agent in CKD 3-5D patients

Material and Methods: A prospective case control study will be done during the period from Feb 2018 – July 2019. 40 patients of stage CKD 3-5D will be evaluated for the effect of antiresorptive therapy in form of oral alendronate. who wil be compared with another control group 40 patients of CKD 3-5D who will not receive alendronate. Effect of antiresorptive therapy on BMD will be studied using DEXA scan at 6 and 12 months follow up.

Clinical significance: The role of antiresorptive therapy should be considered in patients with CKD3-5D, as it affects BMD and decreases the incidence of osteoporosis.

Keywords: CKD, BMD, Antiresorptive therapy.

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled "**TO STUDY THE PREVALENCE OF OSTEOPOROSIS AND THE EFFICACY AND SAFETY OF ANTIRESORPTIVE THERAPY IN CKD3-5D PATIENTS**" exist in the Department of Nephrology, Dayanand Medical College& Hospital, Ludhiana and will be provideo to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

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Place.

Date

APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA

Name of Candidate	Dr. Sudhir Mehta
Department	Nephrology
Topic of Thesis	**TO STUDY THE PREVALENCE OF OSTEOPOROSIS AND THE EFFICACY AND SAFETY OF ANTIRESORPTIVE THERAPY IN CKD3-5D PATIENTS**
Likely date of appearing in PG exam	May 2020
Date of enrolment	21st October 2017
Name of Head of Department	Dr Vikas Makkar
Supervisor	Dr. Vikas Makkar
Co-supervisor	Dr Parminder Singh Dr. Preet Mohinder Singh

Signatures of Members of Research Committee with Stamp	**Signatures of Members of Ethical Committee with Stamp**
1. HOD Pharmacology	1. HOD Physiology
2 HOD Surgery	2 HOD Pathology
3 HOD Pathology	3 HOD Pharmacology
4 HOD Medicine	4 HOD SPM
5 Dean Academics	5. HOD Medicine
6. Vice Principal	6. HOD Surgery
	7 HOD Obst. &Gynae
	8 Legal Expert
	9. Secretary, IEC
	10 Dean Academics
	11 Vice Principal
	12 Principal
Approved: Yes/No	**Approved: Yes/No**
Chairperson, Research Committee	**Chairperson, Ethics Committee**

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr SUDHIR MEHTA 1556/9 Ambala City. Haryana
2	NAME OF THE INSTITUTE	Dayanand Medical College. Ludhiana.
3	COURSE OF STUDY AND SUBJECT	D M.. Nephrology
4	DATE OF ADMISSION OF COURSE	21st October 2017
5	TITLE OF THE TOPIC	TO STUDY THE PREVALENCE OF OSTEOPOROSIS AND THE EFFICACY AND SAFETY OF ANTIRESORPTIVE THERAPY IN CKD3-5D PATIENTS.

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

CHRONIC KIDNEY DISEASE - MINERAL AND BONE DISORDER (CKD-MBD)

Changes in bone and mineral metabolism occur early in the course of CKD. The prevalence of low bone mineral density (BMD) and osteoporosis increases with greater severity of chronic kidney disease (CKD). These changes are called Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD), which includes renal osteodystrophy, extraskeletal (vascular) calcification related to abnormalities of bone mineral metabolism and excessive mortality. Renal osteodystrophy is the component of CKD-MBD that is identified and quantified through bone histomorphometry and includes osteitis fibrosa (hyperparathyroidism), adynamic bone disease and osteomalacia. Several factors related to the pathophysiology of CKD-MBD have been described as markers of increased cardiovascular risk and mortality in these patients, such as hyperparathyroidism, increased FGF-23 (Fibroblast Growth Factor-23) and metabolic acidosis. Metabolic disturbances associated with CKD are increased PTH, decreased 25-hydroxyvitamin D decreased calcitriol, increased FGF 23, Metabolic acidosis, increased bone alkaline phosphatase, hyperphosphatemia (late disorder), Hypocalcemia (late disorder), increased FGF-23 (fibroblast growth factor-23). The elevation in serum PTH is observed from early stages of CKD and results in increased bone resorption in order to maintain calcium balance. Chronic PTH hypersecretion is related to high turnover bone disease, with increased risk of fractures and bone deformities. Several factors contribute to

hyperparathyroidism. The decreased pool of functioning nephrons results in limited capacity for calcitriol production (the active form of vitamin D), due to the smaller amount of 1α-hydroxylase, the enzyme responsible for the conversion of 25-hydroxyvitamin D (25OHD) in its active form. CKD patients, even at early stages of the disease, also have a higher prevalence of vitamin D insufficiency/deficiency than that found in the general population. The decrease in intestinal calcium absorption leads to PTH hyper secretion. The reduced expression of vitamin D receptor (VDR) and calcium-sensitive (CaR) receptor, increasing bone resistance to PTH action and stimulating its secretion, is also observed.

FGF-23 is a phosphatonin produced by osteoblasts and osteocytes which rises very early in CKD to counterbalance phosphate retention. FGF-23 causes inhibition of 1α-hydroxylase, contributing to reduced calcitriol synthesis and to secondary hyperparathyroidism. Increased serum phosphate further reduces calcitriol synthesis and can precipitate in vessels and soft tissues with calcium, reducing the ionized calcium fraction (indirectly stimulating the PTH secretion).

Chronic metabolic acidosis occurs early in the course of CKD and can lead to bone fragility in several ways: increased secretion and resistance to PTH, increased osteoclastic activity, increased renal elimination of calcium, bone mineral dissolution and malnutrition.

Most large-scale studies to determine the effectiveness and safety of osteoporosis drugs or Antiresorptive therapy in the general population did not include patients with severe renal impairment (GFR < 30 ml/min/1.73 m2) as their safety was concern in severe renal impairment. The consensus-KDIGO

2012 reports safety and efficacy of these drugs in patients with CKD 1-3 without evidence of CKD-MBD but does not guarantee their use in patients with GFR < 30 mL/min/1.73 m2, or those with metabolic disturbances of CKD-MBD, recommending to assess the potential benefit to risk of the prescription in this population. But recent studies and new RCTs recommended the safety and benefit of various anti resorptive therapies in stage CKD 4-5 also. The recent consensus KDIGO 2017 guidelines also recommended the use of antiresorptive therapy on BMD in end stage renal disease. So this study was done to study the efficacy and safety of antiresorptive therapy in CKD3-5D patients and to study the prevalence of osteoporosis in patients with CKD3-5D

6.2 REVIEW OF LITERATURE

BONE EVALUATION IN CKD

DXA is the main method used in the diagnosis and treatment of osteoporosis in the general population. Klawansky et al.,[1] Jassal et al.[2] and Lima et al.[3] reported positive correlation between GFR and BMD. In 2017 revised KDIGO guidelines on CKD-MBD recommended BMD testing in patients with CKD G3a- G5D with evidence of CKD-MBD and/or risk factors for osteoporosis.

MODALITIES IN TREATMENT

The maintenance of serum calcium, phosphorus and 25OHD within the normal range are recommendations of international consensus **KDIGO** [4] for patients with CKD stages 3-5. Measures such as adequacy of phosphorus and protein intake, use of phosphate binders, vitamin D supplementation with In individuals with severe renal impairment, use of calcitriol, is important to re-establish optimal calcium and phosphorus levels and minimize hyperparathyroidism, but should be prescribed with caution because of the risk of hypercalcemia hyperphosphatemia, vascular calcification and adynamic bone disease.[5] In moderate to severe CKD patients on conservative treatment serum PTH should be maintained in the upper limit (2- 6 times of normality). Moreover, in CKD patients, an accumulation of N terminal portion of PTH, especially in dialysis patients, may overestimate its serum level [6]

Antiresorptive agents

The recent consensus KDIGO 2017 guidelines also recommended the use of antiresorptive therapy on BMD in end stage renal disease [7].

BISPHOSPHONATES

These antiresorptive agents, widely used in the treatment of osteoporosis have been evaluated in patents with low GFR. Most large-scale studies to determine the effectiveness and safety of osteoporosis drugs in the general population did not include patients with severe renal impairment (GFR < 30 ml/min/1.73 m2).[8] Data about the long term use of antiresorptive therapy in people with renal impairment come from two main studies where oral bisphosphonates were used. These antiresorptive agents, widely used in the treatment of osteoporosis, have been evaluated in patients with low GFR.[9] In one study by Miller et al [10], based on an analysis of data from nine placebo controlled clinical trials of risedronate in 8996 osteoporotic women. The women were classified according to their renal function, estimated by their creatinine clearance (CrCl) calculated by the Cockcroft Gault method. Risedronate 5mg daily was shown to be safe and effective in osteoporotic women with mild (CrCl 50-80mL/min), moderate (CrCl 30-50mL/min) and severe (CrCl <30mL/min) age-related renal impairment. These women experienced no increased incidence of adverse events compared with placebo, with an average duration of exposure to risedronate of 2 years. 301 patients who took risedronate were in the "severe" renal impairment group. Whilst the range of CrCl in this group was 13.2-29.9mL/min. Overall it was concluded that risedronate 5mg daily was safe and effective in the studied population, even in those with CrCl of 15-30mL/min.

Jamal et al [11] used data from 6458 subjects from the Fracture Intervention Trial. This was a placebo controlled randomized clinical trial of alendronate in post menopausal women. The renal function was estimated, using Cockcroft

Gault, for these subjects allowing them to be categorized as having severely reduced renal function (CrC <45mL/min) or moderately reduced or normal renal function (>45mL/min). There were 581 women with CrCl <45mL/min (9.9% of the sample). Women with severely reduced renal function who took alendronate had a higher increase in hip bone mineral density (BMD) compared to those with CrCl>45mL/min but similar increases in spinal and femoral neck BMD. The risk of fractures was higher in women with CrCl<45mL/min. Alendronate reduced the risk of fracture compared to placebo regardless of renal function. There was no difference in adverse events between the two groups. Boonenet al [12] evaluated patients with GFR < 35 mL/min/1.73 m2 receiving zoledronic acid and did not describe worsening of renal function. It is noteworthy that all patients included in these studies had no evidence of CKD-MBD. In contrast, nephrotoxicity in patients receiving pamidronate or ibandronate were reported in a review [13]. Miller et al [14] have recently published a review of the literature on the renal safety of bisphosphonate use for osteoporosis. The authors concluded that the benefits outweigh risks; and even in elderly, frail, osteoporotic patients with renal impairment, intravenous bisphosphonate therapy administration in accordance with the prescribing information did not result in long term renal function decline. One concern with bisphosphonate use in CKD patients is the induction of adynamic bone disease, due to the suppression of bone formation, resulting in bone fragility and fractures. Amerling et al [15] studied 13 patients with CKD 2-4 in use of bisphosphonates through bone biopsy, and found that all of them developed adynamic bone disease. Thus,

bisphosphonates are not indicated in patients with evidence of adynamic bone disease or osteomalacia

Denosumab:

Jamal et al [15] evaluated the effects of Dmab on fracture and BMD by level of kidney function in postmenopausal women included in FREEDOM study: the eGFR was 15-29 mL/min in 73; 30-59 mL/min in 2,817; 60-89 mL/min in 4,069 and 90 mL/min or greater in 842. Changes in creatinine and calcium and the incidence of adverse events were similar between groups and did not differ by level of kidney function. Fracture risk reduction and changes in BMD at all sites were in favor of DMAb. Bock and cols.[17] studied patients with GFR ranging from > 80 mL/min/1.73 m2 to kidney failure requiring hemodialysis, after a single-dose of D-mab. The authors found no differences in pharmacokinetics and pharmacodynamics that justified dose adjustment based on GFR. In another 6-month prospective, open-labeled study by Chen Liang 12 patients on hemodialysis with low bone mass (T-score < −1.0 SD), were evaluated for effect of Denosumab on BMD. The BMD was significantly increased in both the femoral neck (mean increase 23.7%±4.0%) and lumbar spine (17.1%± 2.6%) after 6 months of Denosumab

Teriparatide:

This anabolic agent, analogue of PTH, is used to treat osteoporosis, especially in patients with severe disease and multiple fractures.[18] In patients with mild to moderate CKD (GFR 30-79 mL/min/1.73 m2) who had normal serum PTH, teriparatide was effective in increasing BMD and reducing the risk of fractures, and also safe.[19] As increased PTH levels constitutes a contraindication to teriparatide[20], Teriparatide might be useful in CKD

patients with adynamic bone disease where hyperparathyroidism is not the central disorder and in those who underwent prior parathyroidectomy, but few studies have evaluated its use in these conditions.[19,20]

Selective estrogen receptor modulators (SERM)

Selective estrogen receptor modulators was evaluated by Ishani and cols.[21] in patients with mild to moderate CKD

It increased BMD and reduced the risk of vertebral fractures. There were no significant side effects, although an increase in raloxifene plasma levels in CKD patients has been published.[22] One concern is the increased risk of stroke[23] and fatal deep vein thrombosis, which limits its use in patients with increased risk of thromboembolic and cardiovascular diseases as seen in CKD. Bazedoxifene, another SERM approved for osteoporosis treatment, reduced the risk of fractures in patients with mild to moderate renal impairment and was safe.[24] Tanaka et. al.[25] evaluated the efficacy of raloxifene and its effects on bone mineral metabolism in postmenopausal Japanese patients on dialysis. In a prospective, multicentre study, 17 postmenopausal women on chronic hemodialysis with severe osteoporosis (bone mineral density [BMD] ≤2 SD by bone densitometry) were treated with 60 mg/day raloxifene hydrochloride for 12 months. Raloxifene therapy (for 12 months) improved lumbar spine BMD (by 2.6%) in 53% of the patients, while 70% of the control group showed a reduction in BMD (by 4.0%).

6.3 AIMS AND OBJECTIVES OF THE STUDY

1 To study the prevalence of osteoporosis in CKD 3-5D patients

2. To study the effect of antiresorptive therapy on bone mineral density (BMD) in CKD 3-5D patients

3 To assess the adverse reactions of antiresorptive agent in CKD 3-5D patients.

7.1. MATERIALS AND METHODS

- **Duration Study:** Feb 2018 – July 2019
- **Type of study:** Prospective case control study
- **Sample size** A total of 80 patients CKD 3-5D above the age of 18 years will be enrolled in the study
- **Source of Data:** Patients attending OPD, admitted patients from nephrology ward and those receiving dialysis.

7.2 Methods of collection of Data

INCLUSION CRITERIA:

All the patients above the age of 18 yrs with CKD3-5D with informed consent will be included

EXCLUSION CRITERIA:

- Patients who refuse to give consent
- Patients with age < 18 and > 70 years
- Renal transplant recipients
- H/O of previous use Antiresorptive therapy in last 6 months
- Patients on steroids or h/o steroid intake in past.
- Females patients who have taken any hormone replacement therapy or SERM like raloxifine in past 12 months.
- Patients with severe chronic co-morbidity like CLD,COPD, bronchial asthma and malignancy.etc.
- Patient with adynamic bone disease (with PTH < 130 and/or bone specific alkaline phosphatease < 30)

A predefined proforma will be used to collect the whole data. After an informed consent, relevant history taking and physical examination will be

done Relevant investigations related to CKD and BMD will be done. which includes

- Complete Hemogram
- ESR
- Serum creatirine, urea & electrolytes.
- Serum calcium and phosphorus
- Serum alkaline phosphatase
- Uric acid
- Liver function tests
- Vitamin D3 levels
- PTH levels/bone specific alkaline phosphatase
- Urine routine examination
- USG KUB.
- X ray Dorso-lumbar spine lateral view and X ray hands
- Chest X ray
- Echocardiography (if required)
- DEXA scan - At level of lumar spine (L1-L4) , femoral neck and total hip to be done to measure BMD with T score and age matched Z score as per WHO's criteria

  T score at or above -1 SD defined as normal

  T score between -1 to -2.5 SD defined as osteopenia

  T score at or below -2.5 SD. defined as osteoporosis

GFR wil be calculated as per The CKD-EPI equation. as currently recommended by the international consensus KDIGO 2012 guidelines.

Patients of CKD will be staged into following categories.

Categories	GFR (mL/min/1.73 m2)
G1	≥ 90 Normal or high
G2	60-89 Mildly decreased
G3a	45 59 Mildly to moderately decreased
G3b	30-44 Mocerately to severely decreased
G4	15-29 Severely decreased
G5	< 15 Renal failure

Out of tota: 80 enrolled patients, there will be further subdivision into twc sub groups one group of 40 Patients of CKD stage 3-5D, this group will receive antiresorptive therapy in form of oral alendronate This group wil: be compared another group of 40 patients of CKD stage 3-5D who will not receive orat alendronate and will serve as controls. Patients wilt be followed up 6 monthly with all these repeat investigations till completion of study.

Outcome Parameters

Outcome of study will be assessed with help of DEXA scan and X rays.

DEXA scan

This will done at baseline and will be repeated at 6 month and 12months to assess the effect of antiresorptive therapy on the status BMD

X RAYS:

X ray dorso-lumbar spine and X ray hands will be repeated at 6 month and 12 months to look for evidence of any fractures and vascular calcification

Dunng each follow up, patients will also be looked for any severe adverse reactions related to treatment.

7.3 STATISTICAL ANALYSIS

Data will be described in terms of range; mean ± standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. For comparing categorical data, Chi square ($\chi 2$) test will be performed. T test will also be used for comparison between test and control groups. A probability value (p value) less than 0.05 will be considered statistically significant. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 17 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No. Patients included in the study will have to undergo hematological biochemical or radiological investigations as per the protocol. For this patients included in the study will be informed regarding their inclusion and written informed consent will be taken for all the patients included in the study.

7.4 HAS ETHICAL CLEARENCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes, attached herewith.

8. LIST OF REFERENCES

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PROFORMA

Sr. No.

Name Age/Sex **MRD No.**

Indoor/outdoor/dialysis patient

Father/ Husband Name

Address

Phone No

Date of enrolment

Diagnosis

CKD stage

Comorbidities

Past History

Family History

Personal History

Dietary habits

Smoking

Duration

Number of Pack Year

In case of CKD 5D

Duration of dialysis

Mode of Dialysis

Route

Frequency

Treatment history

Signature of Candidate **Signature of Supervisor**

Antiresorptive Therapy

Drug name

Dosage

Frequency

S.de Effects

Date of start of anti resorbtive Therapy

Compliance to treatment

Type of phosphate binder

Dosage/frequency

Erythropiotin therapy

Recombinant Erythropiotin/Darbepoetinalfa

Dose/frequency

Others

General Physical Examination- at time of enrollment

Weight	Height	BMI
Blood Pressure	Pulse	Temperature
Pallor	Icterus	Clubbing
Cyanosis	JVP	LAP

Dermatological examination

Systemic Examination

Respiratory

Cardiovascular

Abdominal

CNS

Signature of Candidate **Signature of Supervisor**

Investigations

Date	0-3 months	3-6 months	6-9 months	9-12 Months
Hb (g/dl)				
TLC(cells/µl)				
DLC				
Platelets (cells/µl)				
ESR				
Urea(mg/dl)				
Creatinine(mg/dl)				
Sodium(meq/l)				
Potassium(meq/l)				
Calcium(mg/dl)				
Phosphorus(mg/dl)				
Alk.Phosphatase(U/L)				
Uric Acid(mg/dl)				
Total Protein (g/dl)				
Albumin(g/dl)				
SGOT(U/L)				
SGPT(U/L)				
GGT(U/L)				
TB/DB(mg/dl)				
iPTH(pg/ml)				
Bone specific ALP(U/L) (if possible)				

Signature of Candidate

Signature of Supervisor

25 (OH) Vit D(ng/ml)

Blood Sugar

- Random(mg/dl)
- Fasting(mg/dl)
- HbA1c(%)

USG KUB

X-ray Dorso-lumbar spine AP/lateral view

CXR-PA view

X ray hand

DEXA SCAN

Lumbar spine

Femur neck

Total Hip

ECG

HbsAg

Signature of Candidate **Signature of Supervisor**

Anti-HCV		
Anti-HIV 1 and 2		
ECHO (wherever possible)		

ADVERSE EVENTS

- Gastrointestinal -E/o of oesophagitis, gastric and duodenal ulcer.
- Cardiovascular
- Osteonecrosis of jaw
- Severe dermatological manifestations
- Any other adverse event
- Hospitalisation

Death

- Cardiovascular cause
- Sudden death
- Infections
- Others causes

Treatment Given	**Date**	**Any Side-effects**	**Any special remarks**

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date _____

I,. . . . .D/o, W/o, S/o..... . . . . . am willing to participate in the study "**TO STUDY THE PREVALENCE OF OSTEOPOROSIS AND THE EFFICACY AND SAFETY OF ANTIRESORPTIVE THERAPY IN CKD3-5D PATIENTS**" The procedure with its complications has been explained to me in local vernacular language I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out of the study any time without assigning any reason.

.. ..

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि

मैं _____ पत्नी/पुत्र/पुत्री _____ निवासी _____ _____ _____ इस शोधकार्य "**TO STUDY THE PREVALENCE OF OSTEOPOROSIS AND THE EFFICACY AND SAFETY OF ANTIRESORPTIVE THERAPY IN CKD3-5D PATIENTS**" में भाग लेने के लिए राजमन्द हूँ। मैं इस शोधकार्य मे भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मै इस शोधकार्य में भाग लेने के सम्बन्ध मे किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और ऐसे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर — रोगी के हस्ताक्षर/अंगूठे का निशान

नाम. — नाम

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____" **TO STUDY THE PREVALENCE OF OSTEOPOROSIS AND THE EFFICACY AND SAFETY OF ANTIRESORPTIVE THERAPY IN CKD3-5D PATIENTS**" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ ਮੈ ਇਹ ਵੀ ਜਾਣਦਾ ਹਾਂ / ਚਾਹੁੰਦੀ ਹਾ ਕੇ ਉਹ ਰਜਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂੰ ਕਿਸੇ ਵੀ ਤਰਾ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂੰ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂੰ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂੰ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂੰ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂੰ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਸਮੇ ਆਪਣੀ ਰਜਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਮਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ